DEVELOPMENTAL DENTAL DEFECTS AND PALATAL CONFIGURATIONS IN CHILDREN BORN PREMATURELY WITH VERY LOW BIRTH WEIGHTS

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DEVELOPMENTAL DENTAL DEFECTS AND PALATAL CONFIGURATIONS IN CHILDREN BORN PREMATURELY WITH VERY LOW BIRTH WEIGHTS

by

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A thesis submitted in partial fulfilment
of the requirements for the degree of

MASTER OF DENTAL SCIENCE
in
Dentistry for Children

Department of Social and Preventive Dentistry

UNIVERSITY OF QUEENSLAND

June 1984

ACKNOWLEDGEMENTS

I am grateful to my supervisor, Dr J. P. Brown, and the Dean of Dentistry, Professor K. F. Adkins, for advice and encouragement.

I am also indebted to Drs D. I. Tudehope, M. O'Callaghan, C. Souvlis and G. Staples for contributing to the success of this study.

I would also like to thank Ms Joanne Aitken for verifying the statistical data, Mr D. Lund for the excellent photographs and Mrs Paddy Carter for careful typing of the thesis.

PREFACE

Three separate topics were investigated in this thesis, namely, developmental dental defects in neonatal rickets, the effects of trauma from the laryngoscope on the developing dentition in the neonate and the effects of laryngoscopy on palatal configuration.

The plan adopted in this thesis is to report on each area of investigation separately, for clarity. An inevitable consequence is that there is some repetition of the material. The substantive areas of interest are preceded by a chapter revealing the relevant literature, and another describing the patients and general methods used in the research. A final chapter incorporates all the research findings together with the appropriate conclusions.

Three publications have issued from the study, as listed below:

Seow, W.K., Brown, J.P., Tudehope, D.I., O'Callaghan, M. (1984). Developmental defects in the primary dentition of low-birth-weight infants: adverse effects of laryngoscopy and prolonged endotracheal intubation. Pediatric Dentistry 6:28-31.

Seow, W.K., Brown, J.P., Tudehope, D.I., O'Callaghan, M. (1984). Developmental defects in the primary dentition of children born prematurely with neonatal rickets. Pediatric Dentistry 6:88-92.

Seow, W.K., Brown, J.P., Tudehope, D.I., O'Callaghan, M. (1984). Effect of neonatal laryngoscopy and endotracheal intubation on palatal symmetry in two-to-five year-old children. Pediatric Dentistry (in press).

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ABSTRACT

Increasing survival rates of very-low-birth-weight (<1500g), prematurely born children in recent years have made it possible to study the effects of prematurity and low birth weight on the deciduous dentition. This study found that 79.4% of 63 children born prematurely with very low birth weights had defects in the primary dentition; 55.6% had enamel hypoplasia with or without enamel opacity, and 23.8% had enamel opacities alone.

Although the aetiology of the dental defects in this group of children is complex and multifactorial, the most important and direct factor is probably a disturbance in calcium metabolism encountered in the neonatal period in premature infants. Evidence for this hypothesis is seen in the results of dental examination of a group of 15 children in this study who suffered neonatal rickets as a result of prematurity of birth. All 15 children in this group had enamel defects of the primary teeth, indicating that disturbances in calcium metabolism are associated with dental defects.

This study also examined the local adverse effects of laryngoscopy and endotracheal intubation on the developing dentition and palatal configuration. Trauma caused by laryngoscopy and orotracheal intubation affects mainly the maxillary anterior teeth. Examination of the primary dentition of 63 very-low-birth-weight,

prematurely born children showed that developmental defects of these teeth occurred in 85% of 40 intubated children compared with only 21.7% of non-intubated children, a fourfold difference. Trauma caused by laryngoscopy affects mainly the left maxillary anterior teeth; in the intubated group of children with defects of maxillary anterior teeth, 66.1% of the affected teeth were on the left compared with 33.9% on the right, a twofold difference. Hence traumatic injury caused by laryngoscopy and endotracheal intubation at the critical period of amelogenesis may contribute to defects in the dentition of very-low-birth-weight infants whose dental development already is compromised by derangements of calcium metabolism and other systemic factors.

However, although dental defects were permanently recorded, there were no apparent adverse effects on palatal configuration from the neonatal intubation process when the children were examined at two-to-five years of age. Measurements of stone casts from 31 intubated and 18 non-intubated children revealed no asymmetry of palate and dental arch in the intubated group compared with the non-intubated group. Growth and remodelling of the palate and dental arch can repair any deformation, so that any distortions occurring during the neonatal period were not evident at two-to-five years of age.

CHAPTER ONE

REVIEW OF THE LITERATURE

1.1 Introduction

Prematurely born, very-low-birth-weight (<1500g) infants, suffer a variety of serious medical complications in the neonatal period. Because many of them did not survive previously, comprehensive studies on large numbers of such children had not been possible.

Thus, previous studies on the dentition of premature infants were mainly done on those with higher birth weights. It is not known whether premature children with very low birth weights suffer a higher frequency of dental defects. Furthermore, premature children with very low birth weights are predisposed to rickets of prematurity, a special type of neonatal rickets which results from metabolic and dietary causes. While the dental findings of other types of rickets have been described before, no previous study has been done on the dentition of children with rickets of prematurity. Such a study will help elucidate the complex aetiology of developmental dental defects in the deciduous dentition.

In addition, low-birth-weight premature children are subjected to various medical manipulations in and around the oral cavity during the neonatal period. These traumatic procedures may affect the developing teeth and/or palate but their long term effects are unknown.

With increasing sophistication of neonatal care in recent years, there is an increased survival of prematurely born, very-low-birth-weight (<1500g) infants who are now available for study. This study investigated such a group of infants for the prevalence of enamel defects and examined the effects of laryngoscopy and endotracheal intubation on the dentition and palatal configuration. In addition, the dentition of a group of children with rickets of prematurity was studied. To date, no similar investigations on such a group of very-low-birth-weight premature infants have been done before.

This chapter will review various aspects of normal dental development, the causes of enamel hypoplasia, the medical problems suffered by premature infants, dental findings in rickets and the oral complications of endotracheal intubation.

1.2 Normal Dental Development

As early as the twenty-eighth day of gestation, primary odontogenic tissues have differentiated and can be identified as the dental lamina (Slavkin, 1979). This appears as an epithelial thickening at the lateral margins of the stomatodeum, and proliferates into the underlying mesenchyme at specific locations to form the enamel organs. The first enamel organs to appear are those of the lower primary incisors and initiation of the entire primary dentition occurs during the second month in utero (Kraus & Jordan, 1965).

Once initiation has occurred, an enamel organ proliferates to form the sequential stages histologically identified as the bud, cap, bell (histodifferentiation) apposition and calcification stages.

During development of the enamel organ, a series of cellular changes results in the formation of four distinct layers surrounding the ectomesenchyme, which develop before any enamel formation. These are the inner dental epithelium, the stellate reticulum, the stratum intermedium, and the outer enamel epithelium. Each of these cellular layers has important functions in the development of the tooth germ. The inner dental epithelium differentiates to form ameloblasts, the cells involved in enamel formation, while the stellate reticulum and stratum intermedium provide support and nutrition for enamel formation. The outer enamel epithelium has, in addition to its passive role of containing the stellate reticulum, the role of controlling the exchange of substances between the enamel organ and its environment.

Amelogenesis and dentinogenesis involve the production of specialised cellular layers producing a matrix which is subsequently mineralised with hydroxyapatite. During periods prior to enamel matrix formation, the ameloblasts exert an influence on adjacent mesenchyme to differentiate a layer of cells that will become preodontoblasts, the precursors of dentine-forming cells.

The initiation of enamel and dentine matrix formation occurs only when preodontoblasts have differentiated into odontoblasts and established contact with the ameloblasts of the inner enamel epithelium. The process appears to consist of the following steps (Slavkin, 1979). Firstly, odontoblasts begin secretion of the predentine matrix between themselves and the ameloblasts. This matrix contains vesicles containing RNA that seem to be responsible for inducing alterations in the basal lamina of the ameloblasts. Secondly, matrix vesicles from these preodontoblasts are apposed with the preameloblast basement cell membrane and appear to alter it. This contact and induction stimulate the production and secretion of enamel matrix by ameloblasts. Thirdly, dentine matrix production by odontoblasts occur simultaneously with events in the second step. Enamel matrix is initially deposited at the occlusal or incisal surface of the developing tooth. As this process continues in these regions, additional ameloblasts form apically.

Enamel production occurs in many phases (Weinstock, 1972). The first phase involves the secretion of matrix in the lateral intercellular spaces at the tips of the ameloblasts, compressing the ends of the cells, which are now called Tomes' processes. In the second phase, the ameloblasts and the overlying cells move back, leaving behind honeycomb-shaped depressions which fill with matrix as they retreat. The third phase is a nucleation process where apatite crystals are deposited as ribbons

along the lattice work of matrix fibrils. The nucleation process is rapid, and the full c-axis length of the crystals is attained during the time of secretion of a few microns of matrix. The growth of enamel in the outer axial dimension is slower and is not yet completely understood. During this time, enamel crystallites become larger and matrix is returned to the ameloblasts. The final stage of enamel crystal growth is a slow process by which enamel reaches its final high level of mineral content and, as such, is defined as matured. This process of maturation occurs periodically during stages of amelogenesis and continues after the time the tooth emerges.

According to Kraus and Jordan (1965) the anterior primary tooth germs have undergone histodifferentiation and begun morphodifferentiation during the first six weeks of intrauterine life. The secondary primary molar germs normally appear at about the seventh week. However, calcification for the primary central incisors does not start until fourteen weeks, for lateral incisors at sixteen weeks, for the canine at seventeen weeks, the first molar at fifteen and a half weeks and for the second molar at nineteen weeks.

Considering the fact that only approximately 4μm thickness of enamel is deposited per day on a particular tooth surface, enamel formation is incomplete for all primary teeth at the end of a normal pregnancy lasting approximately forty weeks. After an extensive literature review, Lunt and Law in 1974 suggested several changes to

the original calcification times of primary teeth as suggested by Logan & Kronfeld in 1933. According to Lunt & Law, the amount of enamel formed at birth for the maxillary central incisor is 5/6, lateral incisor 2/3, canine 1/3, first molar occlusal surface plus 1/2 - 3/4 crown height and the second molar occlusal surface plus 1/5 - 1/4 crown height. The amount of enamel formed for the mandibular primary teeth are: central incisor 3/5, lateral incisor 3/5, canine 1/3, first molar occlusal surface and second molar occlusal surface are incompletely calcified.

Infants born prematurely will have less enamel formed at birth, the actual amount present will generally vary proportionately with gestational age.

1.3 Classifications of Developmental Enamel Defects

Developmental defects of the enamel can result from disturbances in matrix deposition or in its mineralisation during amelogenesis. These disturbances may be clinically obvious or they may be detected by microscopic means only. Developmental enamel defects may arise from inherited or non-inherited causes. They may be localised, affecting single teeth or multiple teeth, or generalised, affecting groups of teeth developing at the period of disturbance.

Hypoplasia is defined as a quantitative defect of enamel visually and morphologically identified as

involving the surface of the enamel (an external defect) and associated with a reduced thickness of enamel (F.D.I. Commission on Oral Health Research and Epidemiology, 1982). Hypoplasia is thought to occur from local or systemic factors that interfere with normal matrix formation (McDonald & Avery, 1978).

The defective enamel may present in three ways:

(a) shallow or deep pits arranged horizontally in a linear fashion across the tooth surface or generally distributed over the whole or part of the enamel surface;

(b) small or large, wide or narrow grooves;

(c) partial or complete absence of enamel over small or considerable areas of dentine.

Opacity is defined as a qualitative defect of enamel identified visually as an abnormality in the translucency of enamel (F.D.I. Commission on Oral Health Research and Epidemiology, 1982). This defect is thought to arise from factors that interfere with calcification and maturation of the enamel (McDonald & Avery, 1978). An opacity is usually characterised by a white or discoloured (cream, brown, yellow) area but in all cases the enamel surface is smooth and the thickness of enamel is normal, except in some instances when associated with hypoplasia.

Although it may be clinically important to differentiate between hypoplasia and hypocalcification,

the actual distinction may be untenable when adequate investigations are undertaken (Hals, 1962).

Combinations of hypoplasia and opacities can occur on the same tooth surface. They may be quite distinct from each other, i.e. separated by normal enamel, or as a composite lesion composed of an adjacent opacity and hypoplasia.

1.3.1. Inherited types of enamel defects

Two types of inherited enamel defects occur. Those that occur unassociated with evidence of systemic disease are collectively known under the title of amelogenesis imperfecta. Since the introduction of the term by Weinmann, Svoboda and Woods (1945), a number of genetically distinct varieties have been reported, based mainly on their clinical and radiographic appearances. A review by Rao and Witkop (1971) lists eleven varieties and suggests that additional types may exist. The prevalence of all types of amelogenesis imperfecta in the general population is about 1 in 14,000 (Winter & Brook, 1973). Table 1.1 shows the various types of amelogenesis imperfecta and their modes of inheritance.

The second type of inherited enamel defect occurs in association with a number of generalised clinical syndromes of genetic origin. Many of these syndromes result from a defect in the ectodermal tissues, e.g. ectodermal dysplasias and epidermolysis bullosa dystrophica.

Table 1.1 Classification of amelogenesis imperfecta (Winter, G. B. & Brook, A. H.: Dental Clinics of North America, 4:19, 1975)

Hypoplasia	
Type I	Autosomal dominant thin and smooth hypoplasia with eruption defect and resorption of teeth
Type II	Autosomal dominant thin and rough hypoplasia
Type III	Autosomal dominant randomly pitted hypoplasia
Type IV	Autosomal dominant localised hypoplasia
Type V	X-linked dominant rough hypoplasia
Hypocalcification	
Autosomal dominant rough hypocalcification	
Hypomaturation	
Type I	X-linked recessive hypomaturation
Type II	Autosomal recessive pigmented hypomaturation
Type III	Snow-capped teeth
Hypomaturation-hypoplasia with taurodontism	
Type I	Autosomal dominant hypomaturation with occasional hypoplastic pits and taurodontism
Type II	Autosomal dominant hypomaturation with thin hypoplasia and taurodontism

Others result from a defect of both ectodermal and mesodermal tissues such as the tricho-dento-osseous syndrome and Ellis van Creveld syndrome. Inherited metabolic diseases such as phenylketonuria, porphyria and pseudohypoparathyriodism are also often associated with enamel defects of metabolic origin.

1.3.2. Non-hereditary developmental defects of the enamel

During the process of enamel production, the ameloblasts are extremely sensitive to local or systemic injury. Because they are specialised cells, once they are severely damaged, the production of enamel is permanently impaired. Enamel defects are thus irreversible and therefore provide a permanent record of any local or systemic injury occurring during the time of dental development. Knowledge of the chronology of development of the primary and permanent dentitions, as shown in Figure 1.1, allows for dating of these injuries. The position of the junctions between normal and abnormal enamel denotes the duration of injury, and the severity of the hypoplasia may relate to the degree of injury received.

1.4 Systemic Causes of Enamel Defects

Systemic insults to the developing primary teeth may occur prenatally, neonatally or postnatally.

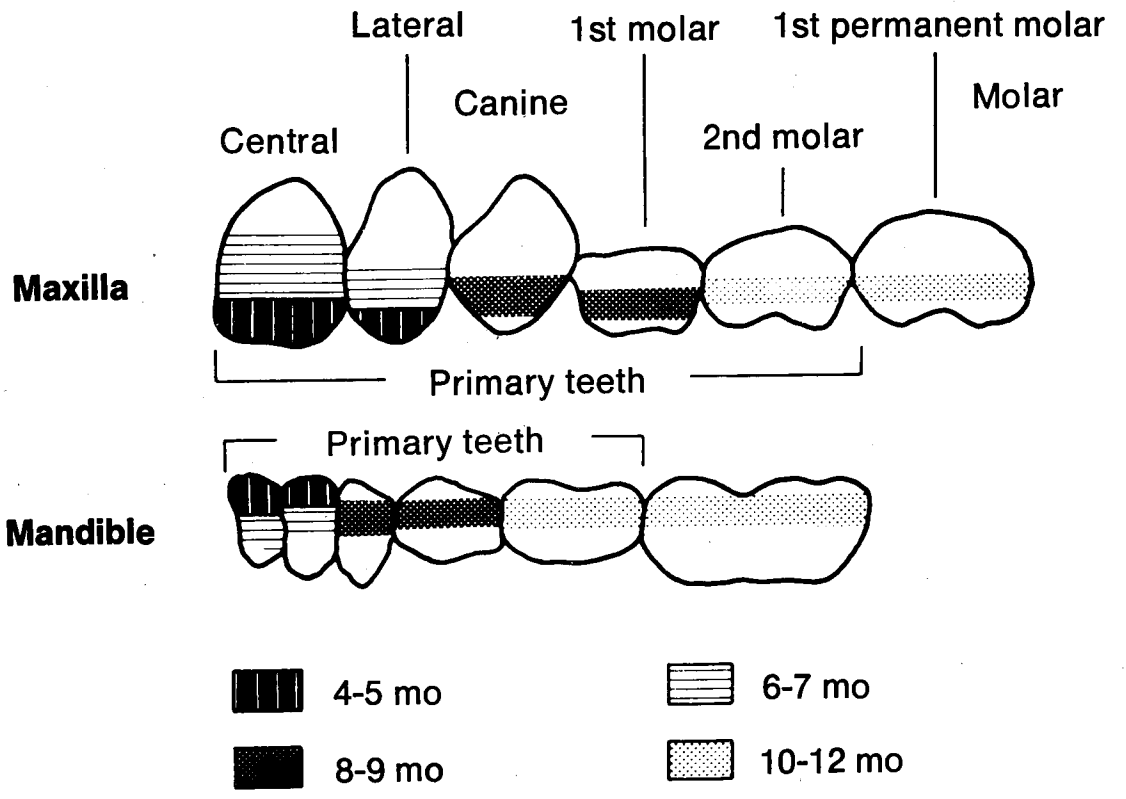

Figure 1.1 Chronology of tooth calcification

(from Via, W. F. and Churchill, J. A., J. Amer. Dent. Assoc., 59:702, 1959).

In contrast, because the permanent dentition mainly develops after birth, its developmental enamel defects are largely caused neonatally and postnatally.

Table 1.2 lists the various systemic factors associated with enamel hypoplasia as have been described in the dental literature. As seen from the table, the factors are diverse and may be classified as birth trauma, infections, nutritional disorders, metabolic disorders and chemicals. However, although the relationship between these causative factors and enamel hypoplasia have been well described, the actual mechanisms of tissue damage are not well understood. There are other conditions associated with enamel hypoplasia for which causal relationships are not established.

1.4.1 Prenatal factors

1.4.1.1 Maternal infections

Maternal infections, such as syphilis and rubella, are associated with severe involvement of the major organs of the fetus. Hence, it is not surprising that enamel hypoplasia is frequently reported in these conditions. It is most likely that the hypoplasia is the result of direct cellular injury by the infecting organisms, although secondary systemic insults could arise from malfunctions of the major organs affected. In addition, the febrile state accompanying many infections may cause ameloblastic derangements (Kreshover & Clough, 1953).

In congenital syphilis, notching of the incisal edges and tapering of the proximal surfaces

Table 1.2 Systemic Factors associated with Enamel Hypoplasia

	Prenatal	Perinatal	Postnatal
(1) Birth Trauma		Breech presentation, multiple pregnancy, Caesarian section, prolonged labour	
(2) Infections	Maternal infections, e.g. Syphilis, Rubella, Measles, Chicken Pox	Congenital Syphilis, Congenital Rubella	Measles, Chicken Pox, Scarlet Fever, Pneumonia, Gastro-intestinal infections
(3) Metabolic Diseases	Maternal hypoxia, Toxaemia of pregnancy, maternal diabetes	Hyperbili-rubinaemia, Neonatal asphyxia. Hypocalcaemia, prematurity complications	Hypothyroidism, Hypopara-thyroidism, Congential cardiac diseases, Gastrointestinal malabsorption, Nephrotic syndrome, chronic renal failure, Biliary atresia
(4) Nutritional Disorders	Maternal vitamin D deficiency	Vitamin D deficiency	Vitamin A or D deficiency
(5) Chemicals	Tetracycline, Thalidomide	Tetracycline	Tetracycline, Lead intoxication, excessive fluoride

of the upper central incisor (Hutchinson's incisors) as well as the abnormal occlusal surface of the molars (mulberry molars) are well documented (Fiumara & Lessell, 1969). Hypoplasia in the primary dentition has also been described (Brauer & Blackstone, 1941; De Wilde, 1943). Similarly, in congenital rubella, hypoplasia in both primary and permanent dentitions has also been documented (Guggenheimer, Nowak & Michaels, 1971; Musselman, 1968; Evans, 1944). However, Grahnen in 1958 reported no clinically detectable defects in his sample of Swedish children.

1.4.1.2 Maternal metabolic and nutritional diseases

Maternal diabetes and hypertension are thought to be associated with an increased incidence of enamel hypoplasia in the primary dentition (Grahnen & Edlund, 1967; Kreshover, Clough & Bear, 1958; Via & Churchill, 1959). However, it is not known whether the hypoplasia results from the metabolic disturbances themselves or from neonatal hypocalcaemia commonly associated with these conditions.

Maternal vitamin D deficiency is also associated with enamel hypoplasia (Purvis, et al., 1973), probably also through a hypocalcaemic effect.

Maternal hypoxia has been reported to cause

disruption of amelogenesis in rat fetuses (Via & Churchill, 1959), but whether corresponding findings are observed in humans is not known.

1.4.1.3 Chemicals

Tetracyclines

Effects of tetracycline antibiotics were widely appreciated only in the early 1960s (Owen, 1963), though earlier reports were made (Schwachman & Schuster, 1956). It also became clear that tetracyclines given after the eighth week of pregnancy pass through the placenta and result in discolouration and hypoplasia of the developing fetal primary dentition. Nylen, Omnell and Loefgen (1972) suggested that tetracyclines achieved their principal effect by injuring presecretory or secretory ameloblasts. Baker (1972), however, focused attention on the disorientation of the matrix and irregularities of mineralisation caused by tetracyclines entering the organic matrix. He also suggested that the drug may impair the ability of the ameloblasts to bring about proper mineralisation of the matrix.

In addition, tetracycline behaves as an anion in solution and chelates the calcium to form a firmly bound tetracycline-calcium orthophosphate complex which causes tooth discolouration and fluoresces with ultraviolet light (Finerman & Milch, 1963).

Thalidomide, a drug now banned for use in pregnancy because of its teratogenic effects, has also been associated with hypoplasia in the primary dentition (Axrup, D'Avignon & Hellgren, 1966).

1.4.2 Perinatal factors

1.4.2.1 Birth trauma

The neonatal line, first described by Rushton in 1933, is a line of enamel hypoplasia, thought to be the result of the trauma of transition from intra-uterine to extra-uterine life (Kronfeld & Schour, 1939). This line is normally seen microscopically only. However, it can be accentuated by several adverse factors during the neonatal period, making it macroscopically evident (Stewart *et al.*, 1983).

Difficult birth such as breech presentation, prolonged labour, multiple pregnancy and Caesarian section have been associated with enamel hypoplasia (Via & Churchill, 1959; Funakoshi, Kushida & Hieda, 1981). This is not surprising as metabolic derangements occur frequently with difficult birth.

1.4.2.2 Metabolic and nutritional disturbances

(i) Hyperbilirubinaemia: As early as 1912, Thursfield reported green pigmentation and hypoplasia

of primary teeth associated with jaundice and haemolytic disease of the newborn. Further cases have been reported by Losch, Brown and Boyle (1940), Tank (1951) and Grahnen and Granath (1962). Miller (1951) showed that the pigment was located in a band in dentine at the level of neonatal development. An association between kernicterus (bilirubin encephalopathy) and enamel hypoplasia was noted by Watson (1955) and Forrester and Miller (1955). Due to improved methods of medical management of Rhesus incompatibility and other causes of hyperbilirubinaemia, enamel hypoplasia and staining by bilirubin is seldom observed nowadays.

(ii) Neonatal asphyxia: Grahnen, et al., in 1969 studied the effects of neonatal asphyxia on dental development. Using Apgar scores for assessment of asphyxia, these investigators could not find any significant difference in the prevalence of hypoplasia between the group with neonatal asphyxia and the control group. However, in a later study, Grahnen, et al., (1974) reported birth asphyxia as a significant factor associated with enamel hypoplasia.

(iii) Neonatal hypocalcaemia: Gaunt and Irving (1941) proved in animal experiments that deficiency of blood calcium causes severe disturbances of tooth calcification. This is confirmed in the study by

Stimmler, Snodgrass and Jaffe (1973) where all twelve patients with neonatal hypocalcaemia resulting from feeding of unfortified cow's milk preparations, had enamel hypoplasia. The hypoplasia was severe in spite of the fact that low serum calcium levels lasted for only a few days. A microscopic study of such hypoplastic teeth was later done by Levin and Keen (1974) who confirmed that initiation of hypoplasia occurred in the neonatal period.

Grahnen and Selander (1954) showed that there was significantly higher frequency of hypoplasia in a group of children who suffered hypocalcaemic tetany (73 percent) compared with a control group of normal healthy children (3 percent).

(iv) Prematurity: As early as 1936, Stein reported that five out of twelve premature children examined, had enamel hypoplasia in the deciduous dentition. These children were found to have higher caries prevalence and an increased tendency to tooth discolouration. Two years later, Schour and Kronfeld (1938) reported enamel hypoplasia in a child born prematurely. They associated the hypoplasia with brain injury at birth.

In another study on 16 children, born mostly in the seventh month of pregnancy, Stein (1947) found

that eight had macroscopic hypoplasia located in the incisal third of the tooth. He stated that he examined "several hundreds" of full term children as a control group and, amongst these, found only one with enamel hypoplasia in the deciduous dentition. On histological examination of the hypoplastic teeth, he found that the striae of Retzius were accentuated as continuations of the enamel hypoplasia. In this investigation, however, Stein did not describe his method of selecting his subjects and therefore it is difficult to assess the frequency of defects.

Forrester and Miller (1955) found that, of 34 prematurely-born children, seven (20 percent) had severe enamel hypoplasia in the deciduous dentition. The frequency is much higher in Kreshover's study (1958) in which a selected series of 35 babies, varying in age from premature stillborns to infants up to two and a half months were examined. Kreshover et al found histologically that developmental defects were present in 77 percent of the premature babies studied and concluded that abnormalities of odontogenesis were non-specific in nature and related to a variety of causes.

In a study of 68 prematurely-born children with birth weights ≤2500g and a control group of 61 full-term children with birth weight ≥3000g, Grahnen

and Larsson (1958) found that enamel hypoplasia was present in 21 percent of the prematurely-born group compared with only 2 percent of the control group, clearly showing that prematurity was associated with enamel hypoplasia. In this study Grahnen suggested that anaemia, cyanosis and neonatal jaundice which were commonly seen in premature infants were unimportant in the aetiology of enamel hypoplasia.

Rosenzweig and Sahar in 1962 examined 21 prematurely-born Jewish infants and reported that enamel hypoplasia was present in eight of them (23.8 percent). In the matched control group of 80 children, only one child had questionable enamel hypoplasia.

In a later study on premature infants, Grahnen et al., (1974) reported that 22 percent of them had enamel hypoplasia compared with 5 percent of controls. In addition, 21 percent had opacities compared with 10 percent of controls.

On analysis of the medical problems suffered by the premature infants, Grahnen concluded that prematurity per se is not a cause of enamel hypoplasia, rather it is the complications of prematurity that appear to be causative. In contrast to his earlier work on neonatal asphyxia (Grahnen, et al., 1969), Grahnen suggested that birth asphyxia

is an important cause of enamel hypoplasia in his study group. However, as birth asphyxia is associated with neonatal hypocalcaemia (Tsang, et al., 1974), it is possible that the high frequency of enamel hypoplasia had resulted from hypocalcaemia rather than birth asphyxia per se. This had not been considered by Grahnen.

In a study by Funakoshi, Kushida and Hieda (1981), an attempt was made to identify certain factors associated with enamel hypoplasia in a group of premature infants with average birth weights of 1612g. The authors reported that there was no significant difference in the frequency of enamel hypoplasia in the infants whose birth weights were appropriate for gestational age and those who were small for gestational age. However, the frequency was much higher for those less than 34 weeks gestation and in those infants who weighed <2100g at birth. The overall frequency of enamel hypoplasia was 26.9 percent. Although the authors listed several neonatal complications commonly present in premature infants, it was unclear from the study whether any of these had a definite role in the aetiology of enamel hypoplasia.

The recent study by Mellander, et al. (1982) on 91 premature infants with low birth weight, showed that 32 percent such children had enamel hypoplasia and opacities. The only significant factor that the authors could relate to the hypoplasia was a lower intake of breast milk during the first week of life. Another factor considered was idiopathic respiratory distress syndrome; however, infants with this condition also had significantly lower breast milk intake.

Thus, it is apparent from the reports discussed that the prevalence of enamel hypoplasia in premature infants is much higher than in those born full-term. However, it is the view of many authors (Grahnen, 1974; Mellander et al., 1982), that it is not prematurity per se that causes enamel hypoplasia but rather the complications associated with prematurity. As discussed in Section 1.6, the premature infant faces several serious complications in the perinatal period, many of which may be causative factors in the aetiology of enamel hypoplasia. To date, such factors have not been positively identified.

1.4.2.3 Infections and chemicals

The dental effects of congenital syphilis and rubella as well as tetracyclines have already been described.

1.4.3 Postnatal factors

1.4.3.1 Infections

Exanthematous diseases such as measles, chicken pox and scarlet fever have been associated with enamel hypoplasia. This was based on the assumption that as these diseases affect epithelial tissues, the ameloblasts, being ectodermally derived, may also be affected. Experimental evidence reported by Kreshover and Clough (1953) showed that severe changes occurred in the ameloblasts of febrile rats. In addition, Kreshover (1960) later reported that rabbits inoculated with Vaccinia virus showed associated enamel disturbances.

Various clinical reports have supported the above experimental findings indicating that exanthematous diseases (Giro, 1947; Sarnat & Schour, 1942) as well as severe respiratory infections (Giro, 1947; Sperber, 1967) are associated with enamel hypoplasia, if these diseases occurred during the period of amelogenesis. In addition, severe gastroenteritis has also been reported to cause enamel hypoplasia (Smith & Miller, 1979; Infante & Gillespie, 1977; Woodward, et al., 1974). Clinical experience, however, is that many children with a history of severe febrile infections do not show dental developmental defects, so the relationship is not a simple one.

1.4.3.2 Metabolic diseases

In the postnatal period, any severe metabolic disturbances can damage the ameloblasts. Congenital cardiac disease has been associated with enamel hypoplasia (Bouyssou, 1962; Berger, 1978). Similarly, renal diseases such as nephrotic syndrome (Shusterman & Fellers, 1969) and chronic renal failure (Woodhead, Nowak, Crall & Robillard, 1982); as well, liver diseases such as biliary atresia (Belanger, et al., 1982) have been implicated. In addition, endocrine disturbances such as hypothyroidism (Hinrichs, 1956), hypoparathyroidism (Albright & Stock, 1933), pseudohypoparathyroidism (Ritchie, 1965; Pisanty & Garfunkel, 1977) have been reported to be associated with enamel hypoplasia. These are all related to disturbances in calcium metabolism.

1.4.3.3 Nutritional disorders

A specific defect of primary teeth called linear enamel hypoplasia, is common in some under-developed countries (Fraser & Nikiforuk, 1982). The pathophysiology of this type of hypoplasia is undetermined, but many authors have suggested the synergistic action of malnutrition and infection as the most probable causative factors (Sweeney, et al., 1971; Scrimshaw, Taylor & Gordon, 1968).

The prevalence of linear enamel hypoplasia has been reported to be about 42 percent in Guatemala (Sweeney, et al., 1969) and 31 percent in San Blas Islands off the Caribbean coast of Panama (Jelliffe, et al., 1961).

It is conceivable that severe general malnutrition can result in malfunction of ameloblasts; however, deficiency of vitamins A and D as well as calcium must play important roles as these substances are intimately linked with epithelial cell function and calcification processes respectively. The role of vitamin A in amelogenesis was proved by Mellanby (1941) when she showed that deficiency of this vitamin resulted in enamel hypoplasia. Similarly, the importance of vitamin D is clearly shown in children who developed rickets as a result of vitamin D deficiency. These children show a high prevalence of enamel hypoplasia (Mellanby, 1937; Elliot, et al., 1934; Shelling & Anderson, 1936). In addition, in the condition called hereditary vitamin D dependency rickets where there is a failure to form the active metabolite of vitamin D in the kidney, enamel hypoplasia has also been reported (Hall, 1959; Archard, 1971).

In conditions of chronic gastrointestinal malabsorption, e.g. coeliac disease, enamel hypoplasia has been reported (Smith & Miller, 1979). The cause of hypoplasia in this case most probably resulted from secondary vitamin D or A and calcium deficiency as a consequence of malabsorption.

1.4.3.4 Chemicals

(i) Tetracyclines: The effects of tetracyclines on the developing dentition have already been described.

(ii) Lead: A pitting type of enamel hypoplasia has been reported in children with chronic lead poisoning (Lawson & Stout, 1971).

(iii) Fluoride: Black and McKay (1916) first systematically described the endemic effect of mottled enamel which was subsequently attributed to excessive levels of fluoride. The prevalence and severity of dental fluorosis have been shown unequivocally to be determined by the fluoride concentration in the drinking water (Dean, 1938). Other factors such as work load, drinking and cooking habits may also affect the prevalence and severity of dental fluorosis (Nanda, et al., 1974). Industrial pollution

(Roholm, 1937; Moller & Poulsen, 1975) and the consumption of fluoride-rich diets further aggravate the situation (Pu & Lilienthal, 1961; Leatherwood, et al., 1965; Minoguchi, 1970). Exposure to milk powder diluted with fluoride-containing water (Ericsson & Ribelius, 1971; Forsmann, 1977) and the systemic use of certain doses of fluoride tablets commencing shortly after birth (Aasenden & Peebles, 1974) may give rise to dental fluorosis of mild degree.

It is generally accepted that dental fluorosis is more obvious in the permanent dentition although the primary dentition may be affected to a lesser extent in areas where the severity of fluorosis is great. (Babeaux & Zipkin, 1966). Severe dental fluorosis in the primary dentition was observed in areas where the fluoride content exceeded six parts per million, or six times optimal in temperate climates (Smith & Smith, 1935; Forsmann, 1974).

1.5 Local Causes of Enamel Hypoplasia

Enamel hypoplasia resulting from local factors is seen in a single tooth or in a localised group of teeth.

This sign differentiates the "local" type of hypoplasia from that resulting from systemic factors where many teeth are usually affected.

Since Turner (1912) first described a localised type of hypoplasia resulting from infection of primary teeth, many clinical reports have suggested that enamel hypoplasia can result from several local causes.

1.5.1. Trauma to primary teeth

Due to the close relationship between the apices of primary teeth and developing permanent teeth, trauma to primary teeth may result in enamel hypoplasia of the succeeding permanent teeth. According to Andreasen and Ravn (1973), 10 percent of enamel hypoplasia affecting permanent anterior teeth in school children in Copenhagen were due to trauma to the primary dentition. The authors also reported that the type of trauma sustained apparently determines the type and degree of developmental disturbance, with exarticulation and intrusive luxation representing injuries with very high frequencies of developmental disturbances while subluxation and extrusion represent low risk groups (Andreasen and Ravn, 1971; Ravn, 1975; Ravn, 1976). Furthermore, the age at the time of injury is of major importance; thus fewer complications are seen in individuals above 4 years of age than in individuals in the younger age group (Andreasen & Ravn, 1971).

1.5.2. Jaw fractures

Jaw fractures are also associated with enamel hypoplasia of developing teeth present at the fracture line, the frequency of developmental disturbances ranging from 19 to 68 percent (Ideberg & Persson, 1971; Lenstrup, 1955; Ridell & Astrand, 1971).

1.5.3. Oral surgery

Oral surgical procedures can also induce enamel hypoplasia. Even extractions of primary teeth have been known to cause developmental disturbances in the permanent teeth (Williamson, 1966). Furthermore, patients operated for cleft palate show a very high frequency of enamel defects in the primary as well as permanent dentitions. Histologic findings in these cases indicate that the surgical trauma could be a contributing factor (Dixon, 1968; Mink, 1959).

1.5.4. Other forms of trauma

Other forms of trauma which have been reported to cause localised enamel hypoplasia are gunshot injuries (Pindborg, 1970), and electrical burns (Alexander, 1964).

1.5.5. Irradiation

Irradiation has been known to cause enamel hypoplasia (Weyman, 1968), although ameloblasts have been reported to be generally resistant to low levels of irradiation (McDonald & Avery, 1978).

1.5.6. Ankylosis

Ankylosis of primary teeth has also been associated with an increased frequency of enamel hypoplasia in the succeeding permanent teeth (Weiss, 1963; Rule, 1972). The reason for this association is unknown, although it may be speculated that whatever factor caused the ankylosis of the primary teeth may also have caused the enamel hypoplasia of the permanent teeth.

1.5.7. Infections

Periapical infections of primary teeth causing enamel hypoplasia of permanent teeth are also well known (Turner, 1912; McCormack & Filostrat, 1967) and has been confirmed in histological studies by Bauer (1946). Acute osteomyelitis has also been established as a cause of enamel hypoplasia (Pindborg, 1970).

1.6. The Premature, Low-Birth-Weight Infant

A normal human gestation is approximately 40 weeks. The World Health Organisation defines a premature birth as one less than 37 completed weeks' gestation (less than 259 days). Most premature infants would have a birth weight of less than the average birth weight of approximately 3333g, the most premature infants having the lowest birth weights. Newborn infants are classified as low-birth-weight (LW) if they weigh less than 2500g, as very-low-birth-weight (VLBW) if they are less than 1500g and as extremely-low-birth-weight (ELBW) if they are less than

1000g (Swyer, 1981).

However, not all low-birth-weight infants are prematurely born. Some infants are born with low birth weights in spite of normal gestation ages. These infants are classified as small-for-gestational-age infants and are diagnosed as such if their weights are more than 2 standard deviations below the mean.

1.6.1. Potential for survival of low-birth-weight infant

At the Mater Mothers' Hospital, South Brisbane, the incidence of premature deliveries was 6.8 percent in 1982. The survival rates in birth weight groups at the Mater Mothers' Hospital from 1977 to 1982, inclusive, were as follows:

	750g	-	26% survival
750 -	999g	-	55% survival
1000 -	1499g	-	87% survival
1500 -	1999g	-	95% survival
2000 -	2499g	-	98% survival.

Follow up studies of very-low-birth-weight infants in the Growth and Development Clinic at the Mater Mothers' Hospital has shown that 5 percent of babies have physical handicaps and approximately 4.5 percent have significant intellectual and/or neurological handicaps (Tudehope, et al., 1981).

1.6.2 Causes of premature births

The causes of premature births are multiple and in at least 25 percent there appears to be no associated factor which might be held responsible (Hobel, et al., 1973). Known factors include maternal infections by the TORCH organisms (Toxoplasmosis, Other infections including Varicella, Syphilis, Measles, Rubella, Cytomegalovirus and Herpes).

Maternal metabolic diseases such as diabetes and hypertension are other factors associated with fetal prematurity (Gabbe & Mesman, 1977).

Abnormalities of the placenta such as placenta previa (implantation of the placenta in the lower segment, encroaching on to the uterus cervix) and abruptio placentae (premature separation of the implanted placenta) predisposes the fetus to premature birth (Kubli & Kaeser, 1969).

In addition, multiple pregnancies, e.g. twins, as well as uterine anomalies can also cause prematurity (Hobel, et al., 1973).

Fetal factors such as Rh haemolytic diseases, some chromosomal abberations and cardiovascular and central nervous system anomalies are also possible causes of premature births in infants (Hobel et al., 1973).

1.6.3 Special problems of the premature infant

Most organ systems are undergoing continued structural and functional development during the last three months of intrauterine life. Hence a premature infant, born before these major organ systems are fully developed, requires difficult adaption to extauterine life. Major complications are encountered in nearly all organ systems.

1.6.3.1 Respiratory diseases

(i) Birth asphyxia, which results from failure of the newborn infant to expand its lungs and establish effective ventilation and perfusion in the minutes following birth, is an important respiratory problem in infants less than 36 weeks gestation. The immature respiratory centre is the underlying cause, with antepartum haemorrhage, intrauterine infections, breech delivery and protracted labour under general anaesthetic often contributory factors (James, 1964).

(ii) Respiratory distress syndrome: Another important respiratory condition commonly seen in the premature infant is respiratory distress syndrome or hyaline membrane disease. This results from a lack of surfactant (a surface tension lowering agent) in the alveoli, resulting in poor alveolar expansion with impairment of gaseous exchange (Usher, 1971).

Respiratory distress syndrome can result in serious pulmonary complications such as pneumothorax and chronic lung disease (bronchopulmonary dysplasia) as well as intraventricular haemorrhage and neurological complications.

(iii) Other respiratory conditions:

Other important respiratory conditions to which premature infants are predisposed are pneumonia and Wilson-Mikity syndrome or pulmonary dysmaturity (Wilson & Mikity, 1960).

The supportive care of the infant with respiratory distress is standard, regardless of its aetiology, and usually consists of careful monitoring, provision of warmth and oxygen therapy. The amount of oxygen given is carefully monitored to prevent the development of retrolental fibroplasia (retinopathy of prematurity) which occurs if the arterial oxygen tension is excessive (Aranda, et al., 1971). Often, it is necessary to provide assisted ventilation for infants with severe respiratory distress. This is usually achieved by administering oxygen via a face mask, nasal prongs or an endotracheal tube connected to a machine delivering continuous distending airway pressure. A time-cycled mechanical ventilator delivering positive pressure ventilation can also be used.

The most serious complication of respiratory disorders in the neonatal period is in the central

nervous system where hypoxic brain damage can result in neurological and intellectual handicap.

1.6.3.2 Hyperbilirubinaemia

Jaundice can be detected in a newborn if the level of unconjugated bilirubin rises to about 100 µmol/L. Neonatal jaundice is seen in about 85 percent of premature infants in the first week of life. The most common cause for jaundice of prematurity is related to decreased conjugation of bilirubin resulting from liver immaturity (Ackerman, et al., 1970).

Other causes of hyperbilirubinaemia in the neonatal period include neonatal hepatitis, haemolytic diseases, e.g. congenital spherocytosis, glucose-6-phosphate dehydrogenase deficiency, sepsis, hypothyroidism, galactosaemia and obstructive causes such as biliary atresia and choledochal cysts.

Unconjugated bilirubin can pass through the blood-brain barrier and cause death or permanent brain damage with chronic disability. This condition is known as kernicterus (Stern & Denton, 1965).

Treatment of hyperbilirubinaemia consists mainly of phototherapy which degrades unconjugated bilirubin in the skin to non-toxic bilirubin products; exchange transfusions may be required in conjunction

with phototherapy for infants with severe jaundice, especially when due to Rhesus isoimmunization (Stern & Denton, 1965).

1.6.3.3 Patent Ductus Arteriosus (PDA)

Normally the ductus arteriosus is functionally closed by 10 to 15 hours after birth and is anatomically closed by 5 to 7 days of age. In premature infants who sustain birth asphyxia or hypoxia after birth, patency of the ductus arteriosus is common. Twenty-five percent of infants less than 1500g birth weight develop the clinical signs of a patent ductus and half this number develop congestive heart failure (Kitterman, et al., 1972).

The avoidance of hypoxia, overhydration, respiratory distress syndrome and hypocalcaemia in the premature infant decreases the incidence of PDA (Kitterman, et al., 1972). Premature infants with a symptomatic PDA and infants who develop the signs of a PDA whilst requiring mechanical ventilation should have their PDA closed medically or surgically. Medical closure of the PDA with the prostaglandin synthetase inhibitor drugs, e.g. Indomethacin, can be achieved in more than half of the cases (Friedman, et al., 1976). However, in premature infants, the majority of PDAs close spontaneously by the expected delivery date or shortly thereafter (Fyler & Lang, 1981).

1.6.3.4 Intracranial haemorrhage

Intracranial haemorrhage is an important cause of death in premature infants (Towbin, 1968). Those who survive a significant intracranial haemorrhage have a high incidence of chronic handicapping conditions including hydrocephalus, cerebral palsy and psychomotor retardation.

Intracranial haemorrhage results from several factors. Birth trauma resulting from difficult labour or breech presentation is an important cause. Perinatal hypoxia, arteriovenous malformations or coagulopathy are other important causes (Milhorat, 1981).

Treatment may be medical or surgical, depending on the type and cause of haemorrhage.

1.6.3.5 Haemological disorders

(i) Haemolytic disease of newborn: The term is used to include the conditions caused by isoimmunisation, i.e. Rhesus incompatibility, ABO incompatibility and minor blood group incompatibility (Naiman, 1972). Haemolysis results from the interaction of antigens on fetal red blood cells with maternal antibodies, which are usually produced following fetomaternal circulation. These Ig G antibodies cross the placenta into the fetal

circulation causing haemolysis of fetal (and later newborn) red blood cells. The consequences of this are anaemia and excessive production of bilirubin in the neonate. In addition, complications include hyaline membrane disease, hypoglycaemia, hypoalbuminaemia and lung oedema, thrombocytopaenia and disseminated intravascular coagulopathy (Queenan, 1977).

Exchange transfusion is required for infants with high serum bilirubin levels. As the consequences of Rhesus incompatibility can be serious, Rhesus negative women should be screened for Rhesus antibodies at their first antenatal visit and also later on during gestation. As a result of early prenatal diagnosis and prompt management, kernicterus (bilirubin encephalopathy) is now rarely encountered in neonatology (Queenan, 1977).

(ii) Anaemia: Anaemia in neonates can be physiological or pathological. Physiological anaemia, which results from the failure of erythropoiesis to keep up with active somatic growth, is more severe in premature than term infants (Oski, 1981). Pathological anaemia results from haemorrhage or haemolysis. In addition, excessive amounts of blood withdrawn for tests during the neonatal period can often cause "sampling" anaemia in the small, premature infant (Faxelius, et al., 1977).

Anaemia may lead to apnoea or congestive cardiac failure and blood transfusion may be necessary in severe cases.

(iii) Bleeding and coagulation disorders: A high incidence of haemorrhage occurs in the premature infant. This may result from immaturity of clotting mechanisms, haemorrhagic disease of the newborn, disseminated intravascular coagulopathy, thrombocytopenia and inherited disorders of blood coagulation (Hathaway, 1970).

Haemorrhagic disease of the newborn is due to deficiency of normal bacterial vitamin K production in the gastrointestinal tract resulting from the bowel being sterile at birth. Routine administration of vitamin K at birth has resulted in a decline of this disorder (Oski, 1981).

Disseminated intravascular coagulation is characterised by the intravascular consumption of platelets and clotting factors. This results in thrombi deposition in small vessels and the production of a haemorrhagic state. Disseminated intravascular coagulation is recognised as a complication of an increasing variety of neonatal conditions including septicaemia, severe shock, severe birth asphyxia, hyaline membrane disease and TORCH infections (Karpatkin,

1971). Treatment usually consists of management of the underlying disease process and treating the haematological abnormality.

1.6.3.6 Metabolic disturbances

As a result of immature homeostatic mechanisms, metabolic disturbances are common in premature infants. They are prone to hypocalcaemia, hypoglycaemia, hyperglycaemia, hypomagnesaemia, hypermagnesaemia, hypernatraemia and hyperkalaemia.

(i) Hypocalcaemia in the premature infant can occur early or late in the neonatal period (Tsang & Steichen, 1977). Early hypocalcaemia results from immaturity of the parathyroid gland with low plasma parathormone, and is associated with respiratory distress syndrome, birth asphyxia, sepsis and maternal diabetes (Tsang, et al. 1976). Late hypocalcaemia or neonatal tetany is due to the feeding of an unmodified cow's milk preparation with low calcium to phosphorus ratios. There is therefore a relative hyperphosphataemia. With the decreased practice of feeding infants unmodified cow's milk, this form of hypocalcaemia is now rarely seen. Congenital hypoparathyroidism (x-linked recessive inheritance, Di George syndrome) and maternal hyperparathyroidism are other causes of neonatal hypocalcaemia.

Hypocalcaemia results in bradycardia, apnoea, convulsions and, if prolonged and severe, pulmonary hypertension (Tsang, et al., 1973). Calcium gluconate supplements for very-low-birth-weight infants may prevent hypocalcaemia. Neonatal tetany is prevented by feeding breast milk or a modified cow's milk formula with a low phosphate content and calcium/phosphate ratio greater than 1.5 : 1 (Lewin, et al., 1971).

(ii) Hypoglycaemia in the premature infant is usually related to decreased availability of substrate and may be associated with birth asphyxia (Senior, 1973). Other causes are maternal diabetes and inherited glycogen storage diseases (Gutbeilet & Cornblath, 1976).

Hypoglycaemia may cause apnoea, convulsions and coma, which may result in long term handicapping conditions such as mental retardation, convulsions, spasticity and microcephaly.

Treatment of hypoglycaemia consists of early diagnosis and feeding with glucose or dextrose infusion.

1.6.3.7 Other problems of premature infants

Besides the above problems, premature infants are susceptible to a variety of other serious conditions in the neonatal period which can affect their outcome (Usher, 1981). They suffer from thermal instability

and lack primitive survival reflexes such as sucking, swallowing and gagging with a high incidence of milk aspiration. In addition, they are very susceptible to infections such as necrotising enterocolitis, as well as gastrointestinal intolerance. Ophthalmic problems such as retrolental fibroplasia, myopia and strabismus occur commonly as do surgical conditions such as undescended testes and inguinal and umbilical hernias.

1.7 Rickets in the Premature Infant

Rickets can be defined as a failure to mineralise osteoid tissue in the growing animal (Rosenthal, 1983). The causes of rickets are multiple and complex but, in general, four categories can be recognised (Cohn & Roth, (1983). A working classification of the pathogenesis of rickets is presented in Table 1.3. The most common cause of rickets is dietary deficiency of vitamin D and calcium. Other major causes include transport defects of intestinal and renal epithelium, metabolic disorders involving the liver and kidneys and bone matrix defects.

The aetiology of rickets in the premature infant is not well understood but is intimately linked with the metabolism of vitamin D, calcium and phosphate in the perinatal period.

Table 1.3 Aetiologic Classification of Rickets *

Dietary

1. Vitamin D deprivation.
2. Calcium deprivation, e.g. general malnutrition, milk-free diets, prematurity, etc.
3. Phosphate deprivation, e.g. abuse of magnesium-aluminium hydroxides as antacids, prematurity, etc.

Transport

1. Malabsorption
   (a) ↓ vitamin D absorption, e.g. bile salts depletion
   (b) ↓ calcium and vitamin D absorption, e.g. sprue, coeliac disease.
2. X-linked hypophosphataemia.
3. Fanconi's syndrome.

Metabolic

1. Hepatocellular diseases with defective synthesis of 25 hydroxy-vitamin D.
2. Long term anticonvulsant use.
3. Renal cortical diseases with defective synthesis of 1.25 dihydroxy-vitamin D.
4. Autosomal recessive vitamin D-dependent rickets.
5. Prematurity.

Matrix Defect

1. Hypophosphatasia.
2. Metaphyseal dysostosis.

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* The aetiology of rickets of prematurity (neonatal rickets) appears to be multifactorial, involving deficient body stores, dietary factors and metabolic factors.

1.7.1. Metabolism and biological activity of vitamin D

The naturally occurring vitamin D compounds are cholecalciferol and ergocalciferol. Cholecalciferol is obtained from endogenous dermal stores of 7 dehydrocholesterol by ultraviolet radiation, while ergocalciferol is derived by irradiation of ergosterol, a plant sterol.

After absorption from the intestinal tract or derivation by irradiation from skin precursor, cholecalciferol is transported to the liver by a specific serum alpha protein where it is hydroxylated at carbon-25 to produce 25-hydroxycholecalciferol ($25(OH)D_3$) (Belsey, et al., 1974). The biologic activity of $25(OH)D_3$ is several fold greater than that of its precursor.

$25(OH)D_3$ is further transported by a protein to the kidney where further hydroxylation occurs at carbon-1 to produce 1,25 dihydroxycholecalciferol ($1,25(OH)_2D_3$), the biologically active form of vitamin D_3 (De Luca, 1975).

Vitamin D affects gastrointestinal, bone, renal and muscle cell functions (Root, 1976). Intestinal and renal cells are concerned with the transcellular flow of calcium whereas bone and muscle cells employ calcium for specialised functions such as mineralisation and contraction (Kodicek, 1974). $1,25(OH)_2D_3$ increases calcium and phosphate absorption in the small intestine, stimulates resorption of calcium from bone and enhances renal tubular reabsorption of sodium, phosphate and calcium (De Luca, 1972).

Vitamin D and its active metabolites increase the activity of osteoclasts and osteoblasts and may directly control the activity of the osteoid osteoclasts which initiate bone mineral deposition (Rasmussen, 1974). Rasmussen and associates (1974) suggested that the major skeletal effect of $1,25(OH)_2D_3$ and $25(OH)D_3$ is to enhance osteocytic osteolysis and that the calcium and phosphate ions so mobilised act to initiate mineralisation of osteoid and activation of mesenchymal cell differentiation.

The effects of vitamin D are influenced by parathyroid hormone (PTH). The mobilisation of calcium from bone as well as gastrointestinal absorption of calcium are enhanced by the action of PTH. In addition, PTH increases the responsiveness of the renal tubular cells to vitamin D, so that the excretion of calcium and phosphate is decreased (Puschett, Morantz & Kurnick, 1972).

1.7.2 Perinatal vitamin D metabolism

Major advances in the understanding of vitamin D metabolism over the past decade have led to important revision of concepts of the calcium and phosphorus homeostasis of the fetus and the newborn infant (Tsang, 1983).

In the fetus, the main supply of calcium and vitamin D is through the placenta. At birth, the transplacental supply of calcium and vitamin D is abruptly terminated and the infant becomes dependent on an intestinal supply instead (Steichen, Tsang & Gratton, 1980). After birth, in order to restore extracellular calcium

concentrations, it is necessary for the neonate to increase acutely the flux from endogenous calcium stores in bones by about 20 percent, or decrease any extracellular fluid to bone fluxes or increase the exogenous calcium supply. Deficiencies in these homeostatic mechanisms result in hypocalcaemia.

The metabolism of vitamin D in the neonate is still unclear. In experiments with neonatal rats it was found that $1,25(OH)_2D_3$ was absent. Instead hydroxylation occurred at carbon 24 to produce the 24,25 dihydroxy metabolite (Weisman, 1976), which is active for intestinal calcium absorption but not bone mobilsation of calcium (Boyle, Omdehl & Gray, 1973). This may have an overall effect favourable for bone mineralisation.

The obvious dietary source of vitamin D for infants is breast milk. However, whether the amount of vitamin D in human breast milk is sufficient to prevent rickets in the newborn is not certain (Tsang, 1983). Some studies have shown that infants unsupplemented with vitamin D tended to have reduced bone mineralisation compared with those who received supplements (Greer, Searcy & Levin, 1981). On the other hand, Lakdawala and Widdowson (1977) reported that vitamin D is adequately present in breast milk and that breast fed infants do not develop rickets.

Cow's milk is less protective against rickets compared with breast milk as shown by the study of Lapatsanis et al. (1968).

1.7.3. Osteopenia in preterm infants

It had been recognised for many years that small premature infants, especially those under 1000g birth weight, often show abnormalities of bone density developing in the first few weeks of postnatal life (Lewin, et al. 1971; Davis, et al. 1978). The appearances include those previously described in the literature under the names of pseudorickets or rickets of prematurity, and cortical thickening of prematurity (Caffey, 1978). Increasing improvement in neonatal care has resulted in better survival rates of very small premature infants; thus there is an increased recognition of these bone lesions. Some preterm infants may even have fractures and other florid radiological and clinical signs of rickets.

The aetiology of osteopenia in premature infants is diverse and not completely understood. The major portion of the newborn's stores of calcium and phosphate are acquired during the third trimester of pregnancy (Tsang, et al., 1976). A premature infant, born prior to this period, will have missed out on these accumulations.

In addition to low calcium and phosphate stores, defects in vitamin D metabolism resulting from renal and liver immaturity may contribute to the development of osteopenia. Hillman (1975) reported that serum 25(OH)D_3 levels are correlated with gestational age, with premature infants having lower levels. Furthermore, administration of vitamin D in premature infants does not appear to result in increased serum 25(OH)D levels showing that

hepatic hydroxylation may be decreased in prematurity.

In addition, recent studies have shown that in a group of premature infants with rickets, serum $1,25(OH)_2D_3$ concentrations were low despite ingestion of vitamin D_3 and that it was possible to reduce the incidence of rickets of prematurity with two to three times the physiological doses of $1,25(OH)_2D_3$ (Seino, et al., 1981). These workers suggested that there was an impairment of renal 1-hydroxylase activity in preterm infants. Also, the use of high doses of $1,25(OH)_2D_3$ may mean that there was some degree of tissue resistance to $1,25(OH)_2D_3$.

However, Glorieux, et al. (1981) found that vitamin D_3 is well absorbed and metabolised in premature infants. Moreover, Steichen, et al. (1981) found that in rickets of prematurity, serum $1,25(OH)_2D_3$ concentrations were high, showing that renal 1-hydroxylase enzyme is present in premature infants.

Many authors have now proposed that the main aetiological factor in rickets of prematurity is a deficiency of supply of calcium and phosphate rather than a decreased production of active metabolites of vitamin D (Tsang, 1983; Glorieux, et al., 1981; Greer, et al., 1982).

Minton and Steichen (1979) have shown that variable intestinal absorption of calcium depending on postnatal gestational age is probably an important factor. In another study (Greer, et al., 1982) it was reported that preterm infants fed standard cow's milk formulae were

shown to have lower bone mineral content than they had in utero. However, if these infants were supplemented with calcium and phosphorus, their bone mineral content was significantly higher than in those infants receiving standard formulae without supplementation. Similar findings were reported in breast fed preterm infants.

In premature infants with infections, or those with birth asphyxia, as well as those with diabetic mothers, absolute dietary calcium intake is generally poor and may be a factor in causing osteopenia (Tsang, et al., 1976).

1.7.4. Clinical signs of rickets in the premature infant

Craniotabes as well as fractures of the ribs and long bones may be seen in severe cases of neonatal rickets. More often, diagnosis of osteopenia is mainly by radiological criteria.

In a study on premature infants, all under 1000g, Masel et al. (1982) reported that all infants showed some loss of bone mineral, as estimated from humeral cortical cross-sectional area, using the technique of Poznanski, et al. (1980). The authors reported a typical progression of radiographic appearances and suggested a system of staging of the changes, as shown in Table 1.4.

Biochemical findings in neonatal rickets include raised alkaline phosphatase levels, which is usually increased three to four times the normal (Masel, et al., 1982). However, major changes in calcium and phosphate levels are

Table 1.4 Stages of Osteopenia and Rickets in the Surviving Extremely-Low-Birth-Weight Infant (from Masel, et al., 1982)

Stage	Approximate Duration	Definition	Incidence	Mean Age of Detection	Range of Detection
1	10-60 days	Demineralisation in metaphyses of long bones and in the margins of other bones	100%	24 days	7-58 days
2	20-80 days	General demineralisation	67%	40 days	20-78 days
3	60-100 days	Active rickets	44%	83 days	54-103 days
4	70-140 days	Healing rickets	61%	84 days	68-113 days

usually absent, although they may be low in the first few days of life (Binstadt & L'Heureux, 1978). This reflects the infant's ability to maintain chemical homeostasis at the expense of bone mineral.

1.8 Dental Manifestations of Rickets

Although the aetiology of rickets is diverse (see Table 1.3), its general manifestations are fairly similar. Skeletal signs such as craniotabes, enlargement of wrists and ankles, beading of costochondral junctions, bending of the shafts of long bones, lordosis, scoliosis and kyphosis have been well described in the medical literature, and may be seen in rickets of any aetiology (Rosenthal, 1983).

Similarly, the dental manifestations of the various types of rickets are broadly similar, and may present as either defects in the enamel or defects in dentine or both.

The dental manifestations of vitamin D-resistant rickets have been fairly well described (Harris & Sullivan, 1960; Marks, Lindahl & Bowen, 1965; Archard & Witkop, 1966; Soni & Marks, 1967; Via, 1967; Tracy & Campbell, 1968; Gardner & Prescott, 1969; Wihr, 1970; Sauk & Witkop, 1973; Pliskin, et al., 1975). This form of rickets is characterised by its X-linked dominant mode of inheritance and decreased renal tubular reabsorption of phosphate, leading to increased levels of phosphate in the urine and low levels of phosphate in the serum (Fraser & Scriver, 1976).

Most reports of vitamin D-resistant rickets indicate the initial presentation of multiple dental abscesses and fistulae. Enamel hypoplasia has been described (Marks, Lindahl & Bowen, 1965; Soni & Marks, 1967) but it does not appear to be a consistent finding. Radiographic examination usually reveals the pulp chambers to be extremely large, with pulp horns often projecting up to the dentinoenamel junction and the dentine appears thin. Abnormalities of alveolar bone such as an indistinct lamina dura, thinning of cortical plates and lacy trabeculation have been reported (Tracy & Campbell, 1968; Marks, Lindahl & Bowen, 1965), suggesting defective calcification but these are not consistent findings.

The histologic findings in vitamin D-resistant rickets are suggestive of disturbances in calcium and phosphate metabolism during the period of tooth calcification. Typically, the dentine is thin, and consists of large calcospherites or globules of abnormally calcified dentine (Archard & Witkop, 1966). These are separated by wide irregular zones of interglobular dentine (Sauk & Witkop, 1973; Pliskin, et al., 1975). Dentinal clefts, tubular defects or voids in the calcified matrix of dentine occur in the region of the pulp horns. These defects usually extend to the dentino-enamel junction and allow direct invasion of microorganisms into the pulp once the enamel is removed, either through abrasion, minimal decay or restorative procedures.

The above clinical and histological findings are also seen in vitamin D deficiency rickets (Mellanby, 1937; Eliot, et al., 1934; Shelling & Anderson, 1936) as well as hereditary vitamin D-dependency rickets in which there is a failure of the kidneys to form the 1,25 dihydroxy active metabolite of vitamin D (Hall, 1959). However, there is one notable exception. In these two types of rickets, enamel hypoplasia is a consistent finding whereas in vitamin D-resistant rickets, it is rarely present. The reason why this is the case is not known, although Fraser and Nikiforuk (1981) speculated that serum calcium levels may be the determining factor as to whether the enamel is affected in any form of rickets. The authors suggested that the low serum calcium levels which are usually present in vitamin D-deficiency rickets and in hereditary vitamin D-dependency rickets predispose to enamel hypoplasia whereas normal calcium levels which are seen in vitamin D-resistant rickets, allow the enamel to be unaffected. However, this theory does not explain why dentine, also a calcified tissue, should be affected to such a severe extent in vitamin D-resistant rickets.

The dental manifestations of rickets of prematurity have not been reported before. One reason for this could be the fact that this form of rickets is seen mainly in small, very-low-birth-weight infants who are prematurely born. Until recently such infants did not survive long and rickets of prematurity remained somewhat a curiosity (Ecks,1957). However, with vast improvements in neonatal

care recently, more of such infants survive and are available for study. This investigation includes a report of the dental manifestations of rickets of prematurity.

1.9 Oral Complications of Endotracheal Intubation in the Neonatal Period

In the premature, low-birth-weight infant, endotracheal intubation is often required to provide a means of establishing an airway to overcome respiratory distress. The endotracheal tube, which is made of polyvinylchloride, can be passed into the trachea either through the nose or mouth and is taped to the face. The diameter of the endotracheal tube selected for premature infants is usually 2.5 or 3mm, depending on birth weight. Because of the small diameter of the noses of premature infants, endotracheal tubes are usually placed orally in this group of infants. The exposed end of the endotracheal tube is connected to a system of mechanical ventilation which provides the infant with adequate oxygen. Figures 1.2 and 1.3 each show a premature, low-birth-weight-infant with an endotracheal tube in place.

In order to insert the endotracheal tube into the trachea, a laryngoscope is required to expose the

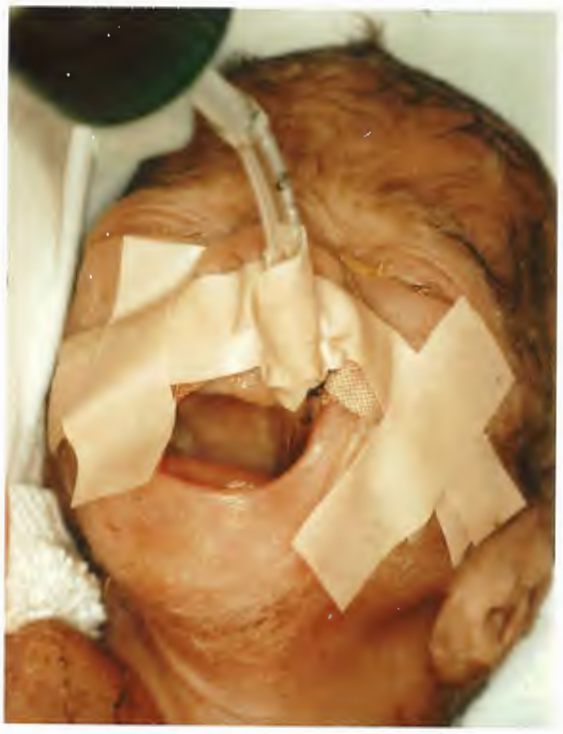

Figure 1.2 A very-low-birth-weight prematurely-born infant with orotracheal tube. Note the pressure exerted on the maxillary alveolar ridge by the tube.

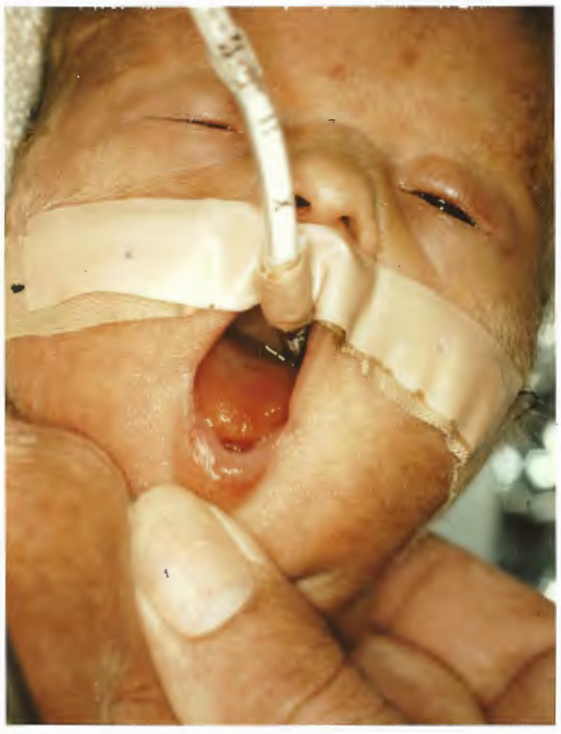

Figure 1.3 A very-low-birth-weight, prematurely-born infant with orotracheal tube. The tube is taped to the upper lip, usually in the midline but this may vary with different operators. The intra oral position of the tube depends on which side the infant is laid.

larynx. In this process, the laryngoscope is inserted into the right side of the mouth, but the blade has to be brought across just to the left of the midline in order to create room for the insertion of the endotracheal tube. The instrument is so constructed that it is always held with the left hand, while the right hand is occupied with the insertion of the endotracheal tube along the groove, which is on the right side of the laryngoscope blade (Brooks, 1982). Ideally, no force should be applied to the maxillary alveolar ridge during the process of laryngoscopy. However, in very small infants, especially those of very-low-birth-weight, the mandible is so hypoplastic and underdeveloped that it does not provide a sufficient fulcrum for lifting the anterior oropharynx and tongue in order to expose the laryngeal opening. Thus a leverage force is sometimes inadvertently exerted on the maxillary anterior alveolar ridge, often causing severe ulceration.

In the newborn, the crowns of the developing anterior teeth and their surrounding dental sacs are in close proximity to the alveolar mucosa; thus they are quite vulnerable to mechanical trauma applied to the alveolar process. Hence, trauma from the laryngoscope or orotracheal tube has the potential to cause dental defects.

1.9.1 Damage inflicted by the laryngoscope

Moylan (1980) reported that in his series of 158 full term children who had mechanical ventilation in the neonatal period, 28 (17.7 percent) had defective deciduous upper anterior teeth. As the upper central and lateral incisors were the teeth most severely affected, Moylan suggested that trauma from the laryngoscope may be responsible for the dental defects. However, 50 percent of the children with dental defects had all four upper incisors affected, which may suggest systemic in addition to local aetiological factors. Furthermore, as no control studies were done, the validity of these results is not firmly established.

Traumatic damage inflicted on erupted teeth by the laryngoscope is a well known complication of general anaesthesia (Wasmuth, 1960; Bamforth, 1963; Rosenberg & Bolgla, 1968; Powell & Keown, 1965; Bunker & Aberdeen, 1962; Henry, 1969). Most reports indicate the upper central and lateral incisors are the commonly affected teeth (Cullen, 1961; Evers, et al., 1967). Damage to these teeth may result in crown fractures, subluxations or even complete avulsions with accompanying danger of aspiration of the teeth into the airway (Powell & Keown, 1965).

Damage to the upper anterior teeth results from levering of the laryngoscope on these teeth during

endotracheal intubation (Evers, et al., 1967). Although this does not occur routinely in general anaesthesia, many patient factors are associated with difficult intubations which lead to leverage forces being exerted on the upper anterior teeth. These factors include small oral cavities, small mandibles relative to maxillas and protrusive upper anterior teeth. In addition, loose and heavily restored teeth are also predisposed to damage.

1.9.2 Damage inflicted by the endotracheal tube

Medical reports have indicated that many iatrogenic complications are associated with endotracheal intubation. These include laryngeal oedema and tracheitis (Jordan, et al., 1970), subglottic stenosis (Hatch, 1968), tracheal stenosis (Fishman, 1969), nasal stricture (Jung & Thomas, 1974), laryngotracheobronchitis and hoarseness (Joshi, et al., 1972) and swallowing of the tube (Flynn & Lowe, 1973).

The orotracheal tube, abutting against the maxillary alveolar ridge, is also a possible local cause of trauma to developing teeth. Sick premature infants with low birth weight require intubation for many days and continual trauma from the orotracheal tube may damage the developing teeth lying beneath the surface of the alveolar ridge.

Boice, Krous and Foley (1976) studied a non-surviving 3-day old low-birth-weight infant who had an orotracheal tube inserted since birth. The authors reported that at autopsy, the left anterior maxillary alveolar ridge exhibited a notable concavity, clearly outlining the site of placement of the orotracheal tube. Microscopic examination of sections taken through the alveolar ridge exhibiting the most severe deformity showed considerable disruption of the enamel organ, with a resultant cystic space around the enamel matrix and deviation of the long axis of the tooth beginning at the cervix. The latter finding appeared consistent with dilaceration of the deciduous left maxillary lateral incisor. Sections taken from the unaffected portion of the alveolar process showed an unremarkable enamel organ with active orderly odontogenesis of the maxillary right deciduous central incisor.

Wetzel (1980) reported that intubated infants may develop a pale, ischaemic area on the alveolar ridge adjacent to the orotracheal tube, and once a small indentation had occurred, the orotracheal tube naturally "slotted"into this defect, giving rise to recurrent trauma and eventual pressure necrosis of the alveolar ridge and underlying tooth bud. He observed that the deepest of these lesions was 7mm deep and divided the alveolar ridge entirely.

Furthermore, Krous (1980) also reported that gingival excavations were prominent in premature infants who had orotracheal intubations compared with those who died shortly after birth. He too suggested that orotracheal intubation was responsible for these gingival excavations as they had contours analogous in size and shape to the orotracheal tube.

In addition to damage to developing teeth, it is also conceivable that damage to palatal shape may occur from prolonged orotracheal intubation. Nowak and Erenberg (1982) recently examined the palates and alveolar ridges of 25 low-birth-weight neonates who had orotracheal intubation and orogastric feeding tubes as well as 35 similar infants who had orogastric feeding tubes only. Compound impressions of the maxilla were taken. The authors reported that 61 percent of those infants who had orotracheal intubation had a palatal or alveolar ridge groove whereas in the group with the orogastric feeding tubes alone, no such grooves were found. They concluded that the use of an orotracheal tube has a deleterious effect on the anatomy of the palate and alveolar ridge in these infants.

It is not known, however, whether such palatal defects are permanent or whether repair and remodelling occurs so that the defect disappears with time. This study also examined the long term effects of orotracheal intubation on palatal and dental arch configuration.

CHAPTER TWO

PATIENTS AND METHODS

2.1 Introduction

To study the effects of prematurity and low birth weight on the dentition, it is necessary to examine a large group of children with gestational ages of less than 35 weeks and birth weights of <1500g. In addition, another group of children who suffered neonatal rickets as a result of their prematurity need to be examined to determine the effects of neonatal rickets on the developing dentition. Such a group of children is usually born very premature with extremely low birth weights, usually <1000g. As survival rates of such infants are low, the numbers in this group of patients are expected to be smaller.

2.2 The Growth and Development Clinic, Mater Children's Hospital

The patients suitable for the present study were available at the Mater Children's Hospital in South Brisbane. In 1978, the Growth and Development Clinic was established at the hospital to provide a multi-disciplinary, longitudinal follow-up of all surviving

infants of very low birth weights (Cleghorn, Tudehope and Masel, 1981; Tudehope, et al., 1981; Masel, et al., 1982; Tudehope, et al., 1983).

The reason for the establishment of the clinic is that premature, very-low-birth-weight infants are considered to be at "high risk" for developmental problems. Thus the benefits of follow-up of such infants include early diagnosis of problems and early intervention which can lead to a better long term prognosis. In addition, evaluation of perinatal factors that have an adverse effect on outcome is possible and methods of perinatal intensive care can be subsequently modified. Furthermore, evaluation of the long term prognosis of high risk populations of infants is possible.

The patients selected for the Growth and Development Clinic are screened regularly for various areas of growth and development, including the physical, social and psychological aspects. However, until the present study, dental development in this group of infants has not been assessed.

2.3 Patient Selection

The patients meeting the requirements of the present study were prematurely-born, with birth weights

of <1500g, and had at least the first deciduous molars, i.e. they were at least two years old. To ensure ready access for the dental examination, only patients living in or near the Brisbane metropolitan area were approached.

For the study on neonatal rickets, it was envisaged that the numbers of infants available would be low. Hence all patients with a definitive diagnosis of neonatal rickets were considered, even though some were residing in country areas.

The patients included in the study did not have any chromosomal abnormalities or congenital malformations of the head and neck such as cleft palates as these are often associated with defective teeth. Children with the rare inherited types of defective dentition, such as amelogenesis imperfecta and dentinogenesis imperfecta, were also excluded. In addition, a history of maternal ingestion of tetracyclines or residence in a naturally high fluoride area excluded a patient from the study, since these have known effects on developing teeth.

Administrative records kept at the Growth and Development Clinic revealed that 86 patients fulfilling the above criteria were available. Eighteen patients with a definite clinical and radiological diagnosis of rickets in the neonatal period were also available for the study on neonatal rickets. Some of the latter group of children have been the subjects of a previous report (Masel, et al., 1982).

Letters were sent out to parents of the above patients, inviting them to join the study (Appendix 1). Sixty-three (73.2%) children presented for the general study. Seventeen (19.8%) letters were returned with "present address unknown" and six (7%) did not present for their examination. Fifteen of the 18 children with neonatal rickets presented for the dental examination. The other three did not reply, probably due to the fact that they were residing in country areas.

2.4 Dental History, Examination and Impression Taking

When a child presented to the clinic, a post-natal medical and dental history was taken using a comprehensive history form (Appendix 2). The examination form (Appendix 3) was used to record both extra-oral and intra oral abnormalities. The teeth present, the type of occlusion and any palatal deformities were recorded. The teeth were dried, and a mirror and probe used to detect caries, opacities and enamel hypoplasia. The diagnosis of opacity was restricted to teeth that showed a marked change in the translucency of the enamel, (with or without colour changes) but with no break in the surface. A diagnosis of hypoplasia was made for teeth showing a break in the enamel surface as detected with a probe (see Figure 3.2). If a tooth showed both opacity and hypoplasia, the diagnosis of hypoplasia was made. All surfaces of each tooth were examined,

and the severity and extent of each dental defect recorded in a comprehensive chart (Appendix 3).

A compound impression, supported on a plastic spoon, was taken of the maxillary arch of all children who were cooperative for this procedure. The impressions were later formed in yellow stone. Impression taking in two-to-four year-old children is not always easy, but this technique has been found to be well tolerated and provided a suitable impression of the palate and the occluso-palatal aspects of the teeth.

Bitewing radiographs were taken only if indicated to assist caries diagnosis and with parental consent.

Intra-oral photographs were taken whenever possible.

At the completion of the examination, the parents were advised on the clinical findings and any dental treatment that was required. Restorative and preventive treatment were offered to children who did not have their own dentist, or if the parent requested it.

2.5 Maternal and Neonatal Histories

Relevant maternal and neonatal histories were obtained from medical records kept at the Growth and Development Clinic, Mater Children's Hospital. This information was entered into the comprehensive history forms after the dental examination had been completed.

2.6 Recording of Dental Defects - Examiner Variability

The examinations were performed by the author; therefore there was no interexaminer variability. The diagnostic criteria described in Section 2.4 allows for clear differentiation between enamel hypoplasia and opacity so that intra-examiner variability is negligible.

2.7 Assessment of Palatal Symmetry

The assessment of palatal dimensions is not an easy procedure due to the complex shape of the palate. For the assessment of palatal symmetry in this study, various devices used by previous investigators were considered but were found to be unsuitable and unavailable. The symmetrograph invented by Korkhaus (1930) transcribes the actual palatal shape in two dimensions onto a piece of paper. However, this machine has to be specially

constructed and the time required to measure one model is excessive. Redman, et al. (1966) used a specially constructed device which can measure the height, width and depth of palates directly in the mouth. This device requires a lot of cooperation from the patient and would not be suitable for the very young patients in our study.

Van der Linden (1978) suggested measurement of dental casts using a three dimensional coordinate system for the spacial location of various reference points on the cast. This appeared to be a direct method of measurement but the device used by Van der Linden (the Optocom) is difficult to use and is not easily available. However, for this study, a machine which employed a similar principle in the measurement of production pieces in engineering was used. This machine, the Olivetti Inspector, was located at the Telecom Workshop at Bulimba, Queensland.

Using this machine, the x, y and z coordinates of selected points on the dental casts were determined. These coordinates of the Cartesian system locate a point in the direction of the horizontal (x coordinate), vertical (y coordinate) and depth (z coordinate) axes. Comparison of the coordinates of the reference point on a tooth with that of the tooth on the other side will reveal any discrepancies of the arch form in the three dimensions. Details of the measurement procedures and validation of the method are described in chapter five.

2.8 Statistical Analyses

Data were analysed using the Chi-square test with Yates' correction or the Student's "t" test to detect differences between the groups, whichever was appropriate.

CHAPTER THREE

DEFECTS IN THE PRIMARY DENTITION OF CHILDREN BORN PREMATURELY WITH VERY LOW BIRTH WEIGHTS AND NEONATAL RICKETS

3.1 Introduction

The type of rickets seen in premature infants (neonatal rickets) appears to be multifactorial in origin, and not completely understood (Tsang, et al., 1977; Root, 1976). As the major portion of the newborn's stores of calcium and phosphate are laid down in the last trimester of pregnancy, a very-low-birth-weight infant (<1500g) born prior to this would have missed these accumulations. Also, liver and renal immaturity result in defective conversion of vitamin D to its active metabolites. Furthermore, there is the difficulty of supplying and ensuring absorption of calcium, phosphate and vitamin D to premature infants.

Although the adverse effect of other types of rickets on the dentition has been well documented (Witkop, 1975), to date, no dental studies have been carried out on children who developed rickets in the

neonatal period. The purpose of the present study is to investigate the dental defects found in a group of extremely-low-birth-weight premature infants with a definite diagnosis of neonatal rickets.

3.2 Patients and Methods

Letters of invitation to join the study were sent to parents of 18 children from the Growth and Development Clinic, Mater Children's Hospital, South Brisbane. These children were aged two years and over and had a definite clinical and radiological diagnosis of rickets in the neonatal period. Most of these patients have been previously reported in the medical literature (Cleghorn, et al., 1981; Masel, et al., 1982). Altogether, 15 patients consented to the study while three did not reply.

All the 15 patients, 11 females and 4 males, were born prematurely, with a mean birth weight of 852g (range 609 to 1028g). The mean gestational age was 27.5 weeks (range 24 to 32 weeks). The mean age of the children at examination was 3 years 7 months (range 2 years 2 months to 4 years 3 months). The patients included a pair of discordant twins and two survivors of a triplet birth. All patients were diagnosed as having rickets in the neonatal period by accepted clinical and radiological criteria and received treatment with dihydrotachysterol,

vitamin D and calcium supplements.

In this series of very-low-birth-weight infants, the clinical features which led to the diagnosis of neonatal rickets included spontaneous rib fractures and/or craniotabes. Biochemical studies were of little value because serum calcium and phosphate levels tended to be within the normal ranges. The diagnosis of neonatal rickets was established by radiological criteria. These included metaphyseal disturbances, periosteal reaction and general loss of bone density. The loss of bone density was determined by measurements of the humeral cortex as described by Poznanski, et al., (1980). Other medical causes of these radiological changes such as osteogenesis imperfecta, hypophosphatasia, Menke's syndrome, congenital syphilis, congenital rubella, etc., were excluded by appropriate laboratory tests, serial x-rays and clinical progress.

The dental examinations were done under ideal conditions at the University Dental School. The teeth were dried and a mirror and probe were used for the detection of caries, enamel hypoplasia and opacities, as described in Chapter Two. Abnormalities of soft tissues were also noted. Bitewing radiographs were taken of four children to assist caries diagnosis. Intra-oral photographs were taken in some children. Postnatal medical and dental histories were obtained from the parents. Maternal and neonatal medical histories were obtained from hospital records.

3.3 Results

The relevant clinical details of this series of 15 children with neonatal rickets are summarised in Table 3.1.

3.3.1 Case Histories

The onset of rickets of all patients in this study occurred during the neonatal period; typical radiological changes were apparent by 14 to 30 days. The duration of the radiological findings varied between 60 and 140 days. There was no correlation between the duration of rickets and the severity of dental defects.

A maternal history of pre-eclampsia was recorded in Case 1 but maternal histories of the other 14 children were non-significant. Medical histories since leaving hospital were non-significant except for Case 2 who developed measles at about 14 months. No clear histories of oral trauma were recorded in our series. None of the children had been to a dentist except for Case 4 who had a dental examination only. The mother of the twins (Cases 5 and 6) was the only mother who ingested fluoride tablets (2.2mg per day) during pregnancy. Only three children (Cases 5, 6 and 15) ingested fluoride tablets and all three started only after the first year of life. None of the subjects drank fluoridated water.

TABLE 3.1. Summary of clinical and dental information of 15 children with neonatal rickets.

CASE NO.	GESTATIONAL AGE (weeks)	BIRTH WEIGHT (gms)	AGE AT EXAM	SEX	DENTAL DEFECTS		OTHER SERIOUS ILLNESSES IN THE NEWBORN PERIOD
					OPACITIES	HYPOPLASIA	
1	29	1020	2yrs 9mths	F	DE	B | B	Moderate RDS, PDA Cholestatic jaundice, gastro-intestinal intolerance.
2	26	850	2yrs 10mths	F	D | D		Moderate RDS, PDA.
3	27	820	3yrs 2mths	F	BA | A DC | CDE	BC	Severe RDS.
4	31	961	4yrs 3mths	M	E | DE	C | AB E	Severe RDS.
5	26	897	3yrs 7mths	M	B | B	A C | C	Apnea of prematurity.
6	26	605	3yrs 7mths	M	B | B A | A	A C | C	Apnea of prematurity.
7	26	866	2yrs 4mths	M	C		Severe RDS, non-specific chronic lung disease.
8	24	609	2yrs 2mths	F		A	Bronchopulmonary dysplasia, gastro-intestinal intolerance.
9	30	913	2yrs 6mths	F	B D | C	A | C	Non specific chronic lung disease, PDA, cholestatic jaundice.
10	26	750	3yrs 9mths	F		B	Moderate RDS, PDA, oesophageal stenosis.
11	26	730	3yrs 9mths	F		C | C	Moderate RDS, PDA.
12	32	1028	3yrs 1mth	F		A	Non specific chronic lung disease.
13	26	880	3yrs 9mths	F	E | E		Moderate RDS, PDA.
14	32	1015	3yrs 6mths	F	D	AB	NEC, prolonged hyperbilirubinaemia.
15	26	840	3yrs 4mths	F		C | AB	Apnea of prematurity.

Abbreviations :

PDA patent ductus arteriosus.

RDS respiratory distress syndrome.

NEC necrotising enterocolitis.

3.3.2 Clinical Findings

Marginal gingivitis was noted in most children but otherwise no soft tissue abnormalities were present.

Every child in our series had a complete primary dentition at the time of examination except for three children (Cases 2, 7 and 9) whose second primary molars were still unerupted.

All 15 children showed defects of the primary dentition. Three children (20%) had only enamel opacities. In seven other children the opacities and hypoplasia were present in different teeth. These opacities which consisted of white or yellow-brown patches were located mainly on the buccal and occlusal surfaces of the teeth.

Of greater interest is the observation that 12 children (80%) showed hypoplasia of at least one tooth. The dental defects of Cases 3 and 4 are shown in Figures 3.1 and 3.2 respectively, and are representative of the more severely affected cases.

Table 3.2 shows the distribution of dental hypoplasia and opacities. The teeth most commonly showing hypoplasia were the primary upper central and lateral incisors followed by the upper and lower canines. On the other hand, the lower first primary molar and canine were the most common teeth showing opacities followed by the lower second primary molar.

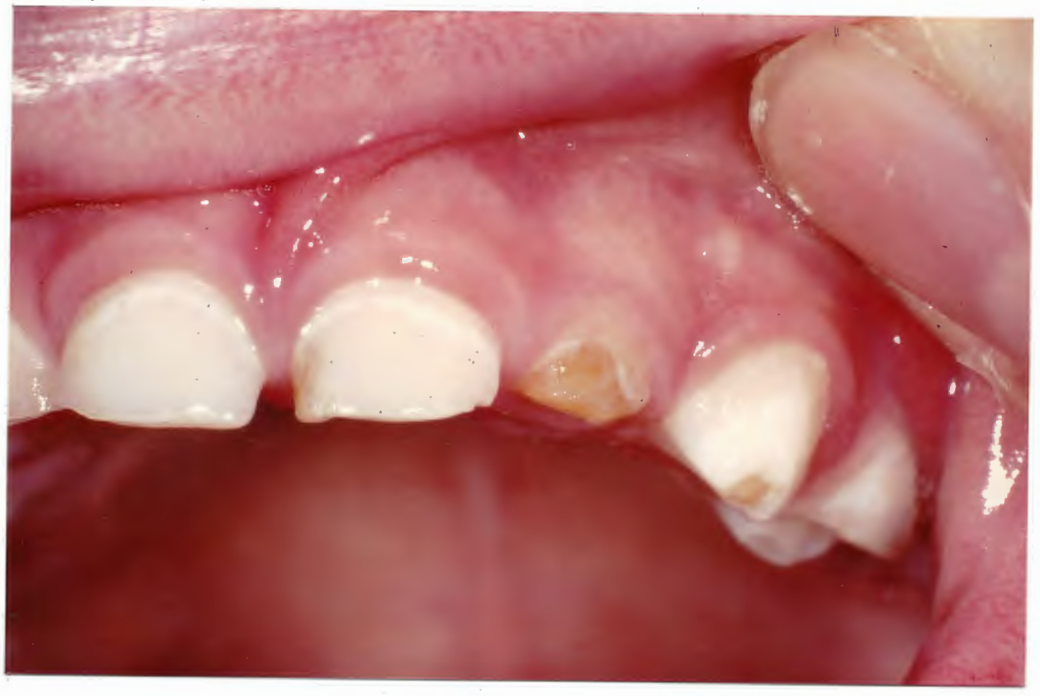

Figure 3.1 Defective maxillary teeth in three year old girl with birth weight of 820g and gestational age of 27 weeks. She developed severe rickets during the neonatal period as a result of her premature birth. (Case 3, Table 3.1).

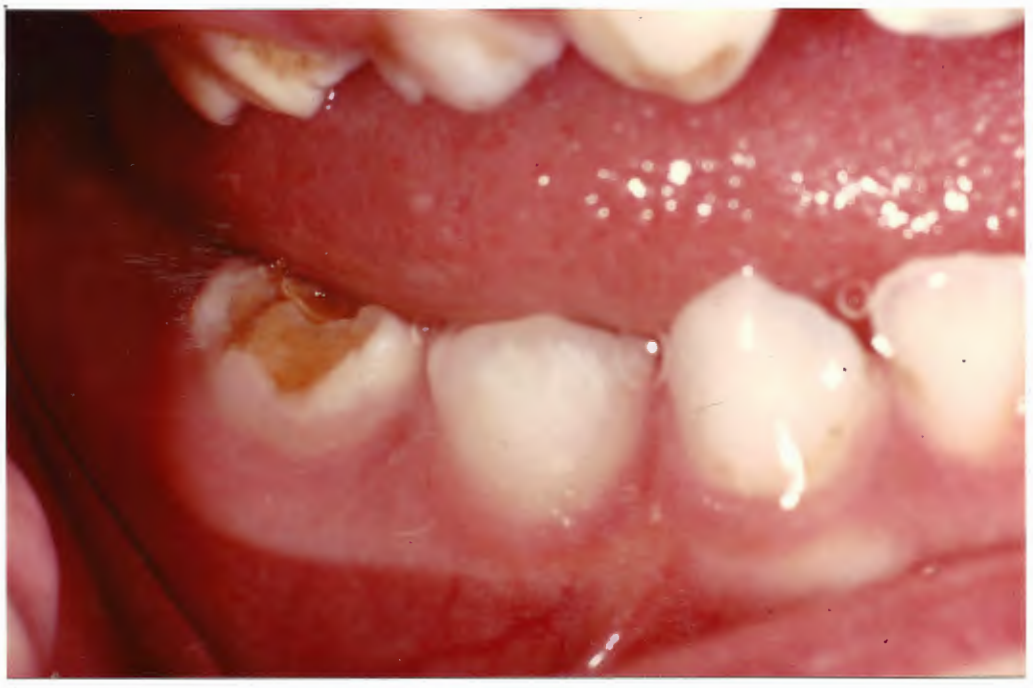

Figure 3.2 Hypoplastic mandibular right second deciduous molar in a four year old boy with birth weight of 961g and gestational age of 31 weeks. Other hypoplastic teeth included the maxillary right deciduous canine and the maxillary left deciduous central and lateral incisors. He had neonatal rickets resulting from prematurity. (Case 4, Table 3.1).

TABLE 3.2: The distribution of dental hypoplasia and opacities in the primary dentition of children with neonatal rickets.

	TEETH AFFECTED*				
	A	B	C	D	E
Maxilla	8(2)	7(4)	4(0)	0(2)	0(2)
Mandible	0(2)	0(2)	4(6)	0(6)	1(4)
TOTAL	8(4)	7(6)	8(6)	0(8)	1(6)

* opacities in parentheses

Depending on location, the hypoplastic defects fell into two main groups. In the first group, the incisal edges appeared fairly intact and the hypoplastic defect appeared as a broad shallow pit or band in the labial surface of the crown. A total of ten teeth in six of these children showed this defect.

In the second group, the hypoplastic defect extended from the incisal edge onto the incisal third or half of the facial surface. This defect was found in 14 teeth of ten children.

Apart from dental defects, additional clinical findings in these children showed that the prevalence of caries was low. The only caries were detected on the occlusal pits of the first primary molars in Case 3.

No discolourations or opacities suggestive of staining by tetracycline, bile pigments or fluoride were seen.

3.3.3 Radiographic Findings

Examination of bite-wing radiographs of Cases 4, 10, 11 and 12 did not reveal any abnormalities of the teeth. The sizes of the pulp chambers were within normal limits and no extensions of the pulp to the occlusal surfaces were noted. The radiographs of Cases 10 and 12 are shown in Figure 3.3.

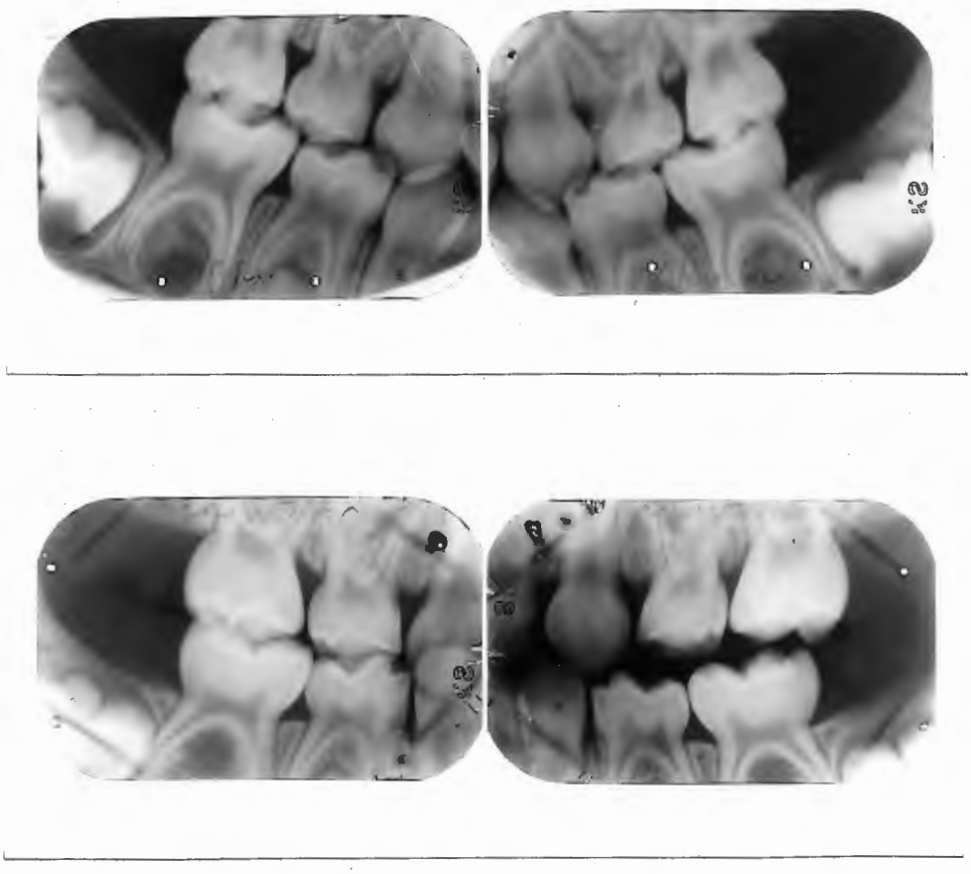

Figure 3.3 Bitewing radiographs of two three-year-old girls who had severe neonatal rickets because of extreme prematurity of birth (Cases 10 and 11, Table 3.1). Note the normal thicknesses of dentine and the normal appearances of the pulp chambers in both cases.

3.4 Discussion

According to Lunt and Law (1974), calcification of the primary dentition begins with the maxillary central incisors at 14 weeks in-utero, but enamel formation of all primary dentition remains incomplete at birth, even for the full-term newborn. Hence, in the premature infant, the amount of enamel laid down will be much less. Since rickets represents a severe disturbance of calcium metabolism, it is reasonable to expect that premature infants with rickets may have developmental defects in their primary teeth. The results of the present studies confirm this expectation; all 15 children had dental developmental defects, either in the form of opacities or hypoplasia of the crown.

Prematurity without rickets has been reported to be associated with an increased frequency of developmental dental defects in the range of 21% to 27% compared to around 2% in full-term infants (Stein, 1947; Grahnen & Larsson, 1958; Rosenzweig & Sahar, 1962; Funakoshi, et al., 1981). These values are well below the 100% frequency in our series of premature infants with neonatal rickets, suggesting that rickets is one of the possible aetiological factors. If systemic influences such as prematurity and rickets are wholly responsible, then it is expected that the defects would be symmetrical, yet they are not (Table 3.1). Possible

explanations for this discrepancy include the modifying influence of local factors, and variation in tissue response of the developing teeth. On the other hand, the distribution of the defects may be symmetrical, but because of the inability of current techniques to detect minor defects, only obvious defects were noted, while clinically inapparent defects were missed.

To the best of our knowledge, no previous studies have been done on the prevalence of developmental dental defects in neonatal rickets. Other types of rickets have been shown to be associated with dental abnormalities (Elliott, et al., 1934; Witkop, 1975), so it is not surprising that this is also the case with neonatal rickets. However, a direct causal effect cannot be proved because the factors of prematurity, low-birth-weight and neonatal rickets cannot be separately analysed, as neonatal rickets is seldom, if ever, seen in infants without these conditions.

Further support for an important role of calcium metabolism in the pathogenesis of developmental dental defects is provided by clinical observations that full-term neonates with hypocalcaemic tetany can

CHAPTER FOUR

DEVELOPMENTAL DEFECTS IN THE PRIMARY DENTITION OF CHILDREN BORN PREMATURELY WITH VERY LOW BIRTH WEIGHTS: ADVERSE EFFECTS OF LARYNGOSCOPY AND PROLONGED ENDOTRACHEAL INTUBATION

4.1 Introduction

Previous studies of the primary dentition in premature infants have demonstrated a high frequency of enamel hypoplasia (Stein, 1947; Grahnen & Larsson, 1958; Rosenzweig & Sahar, 1962; Funakoshi, et al., 1981). However, most of these studies were confined to children with birth weights of 1500g to 2500g, except for the study by Funakoshi, et al., (1981) which included some children below birth weights of 1500g, and the study by Mellander (1982) of children with birth weights of under 2000g. In recent years, increasing sophistication in neonatal care has resulted in greater survival rates for very low-birth-weight infants (<1500g). We therefore recalled 63 such children to determine the frequency of defects in the primary dentition. To date, no similar studies on a large group of comparably low-birth-weight infants have been reported.

develop dental hypoplasia (Stimmler, et al., 1973; Purvis, et al., 1973). Also, conditions such as neonatal asphyxia and maternal diabetes are associated with an increased frequency of neonatal hypocalcaemia and enamel hypoplasia (Miller & Forrester, 1959; Grahnen & Edlund, 1967).

3.5 Conclusions

The results of the present studies show that children born prematurely with low birth weight and neonatal rickets have 100% frequency of defects in the primary dentition. These results, together with supportive evidence of dental abnormalities seen in other forms of rickets and other clinical observations, indicate that deranged calcium metabolism has a possible role in pathogenesis. However, the confounding factors of prematurity and its associated complications cannot be ruled out because neonatal rickets is seldom, if ever, seen in infants without these conditions.

CHAPTER FOUR

DEVELOPMENTAL DEFECTS IN THE PRIMARY DENTITION OF CHILDREN BORN PREMATURELY WITH VERY LOW BIRTH WEIGHTS: ADVERSE EFFECTS OF LARYNGOSCOPY AND PROLONGED ENDOTRACHEAL INTUBATION

4.1 Introduction

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In addition, we also examined the possible adverse effects of endotracheal intubation and mechanical ventilation on the developmental defects in the upper anterior teeth of these children. Two previous reports (Moylan, 1980; Boice, et al., 1976) have suggested that these procedures may have traumatic effects on the developing primary dentition. It is also well known that the laryngoscope can traumatize erupted teeth (Wasmuth, 1960; Bamforth, 1963; Powell & Keown, 1965).

4.2 Patients and Methods

The patients in this study were children aged 2 years and older who were attending the Growth and development Clinic of the Mater Children's Hospital, South Brisbane.

A total of 63 children with very low birth weights were available for study. They were all prematurely born, with birth weights of between 605g and 1500g, and a mean birth weight of 1154g.

There were 37 males and 26 females. Forty received endotracheal intubation and mechanical ventilation in the neonatal period, while 23 did not. At the time of dental examination, the ages of the children ranged from 2 years 2 months to 5 years 5 months, with a mean of 3 years 8 months. All these children were singleton births, except for a set of twins and three sets of triplets, two sets of which had two surviving members each. Only two children from the third set of triplets were included in the study because the third child had a cleft lip and palate and was thus excluded because teeth in the region of oro-facial clefts are often also defective.

The dental examinations were performed under ideal conditions at the University of Queensland Dental School. The teeth were dried and a mirror and probe used to detect caries, opacities and enamel hypoplasia, as outlined in Chapter Two. Intraoral photographs were taken in some children. Postnatal medical and dental histories were obtained from the parents. Maternal and neonatal medical histories were obtained from hospital records.

Data were analysed using 2x2 contingency tables and χ^2 tests with Yates' correction or the Student's t-test to detect statistical differences between groups.

4.3 Results

4.3.1 Prevalence of Dental Defects

Table 4.1 shows the prevalence of developmental dental defects found in the very-low-birth-weight children. A total of 50 children (79.4%) out of 63 had developmental defects of the primary teeth, seen either as opacities or enamel hypoplasia. Fifteen children (23.8%) had only opacities of the primary teeth. These opacities, which consisted of white or yellow-brown patches, were located mainly on the buccal and occlusal surfaces of the teeth.

Of greater interest is the observation that 35 children (55.6%) showed enamel hypoplasia of at least one tooth. The hypoplasia typically presented as either a shallow depression or as a shelf-like defect on the labial surface which usually involved the incisal edge. Figures 4.1 and 4.2 depict the dental defects in two typical cases.

TABLE 4.1 . Frequency of developmental dental defects in very-low-birth-weight children.

	Dental Defect		No Defect	Total
	Hypoplasia	Opacity		
Number of Children	35	15	13	63
Percentage	55.6	23.8	20.6	100

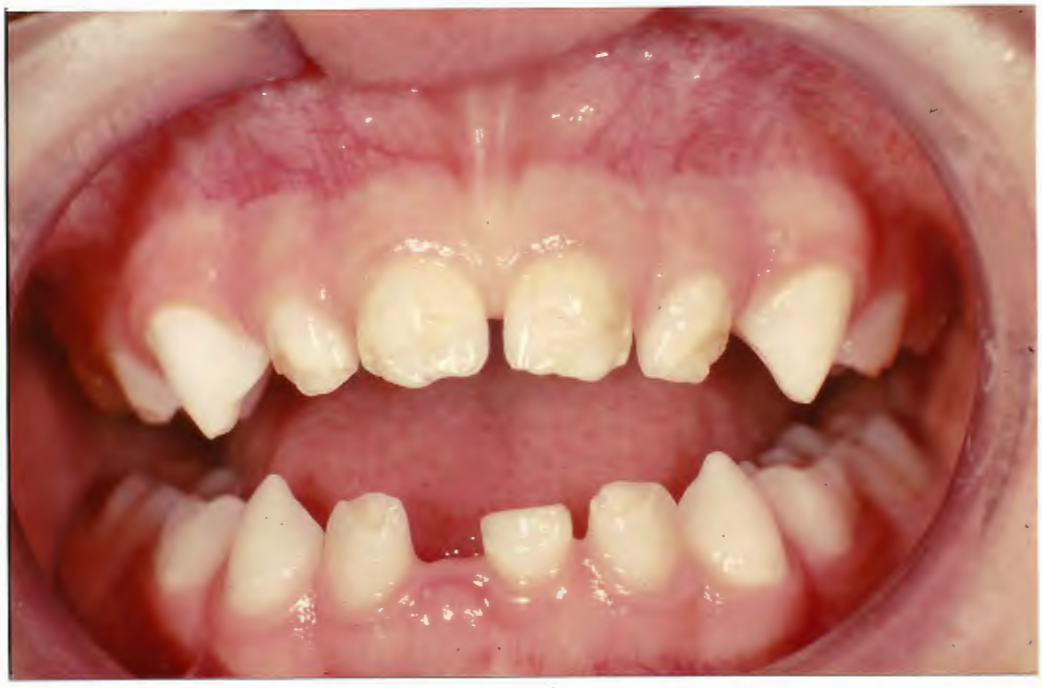


Figure 4.1 Defective dentition of a three year old girl born after 29 weeks gestation with birth weight of 1300g. She developed severe hypocalcaemia in the neonatal period.

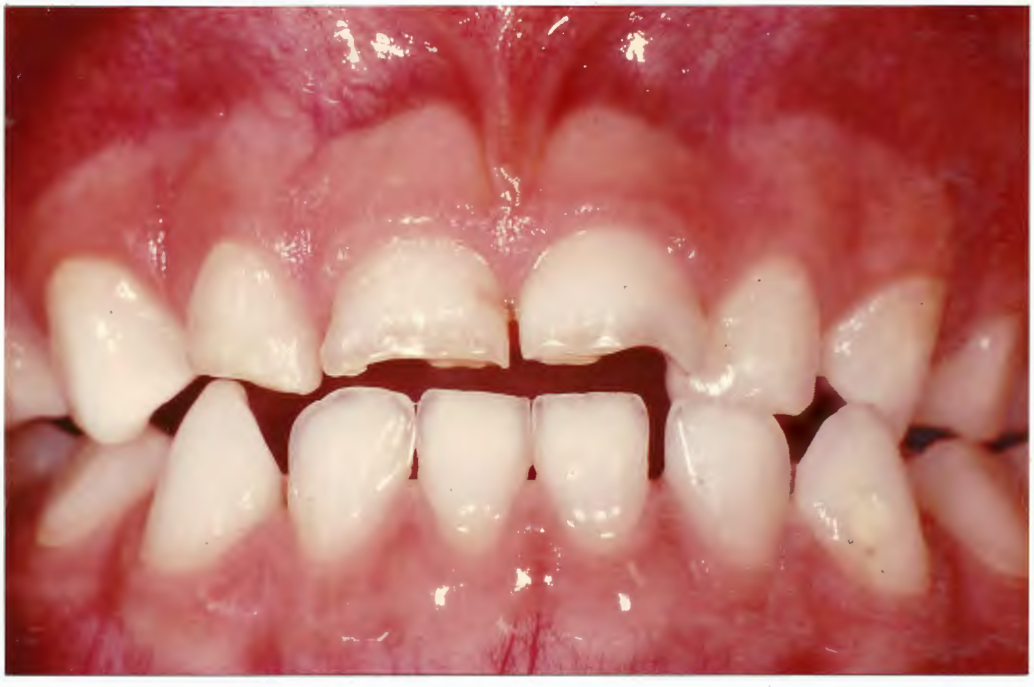


Figure 4.2 Hypoplastic maxillary incisors in a three year old girl with birth weight of 1405g and gestational age of 31 weeks.

4.3.2 Effect of Endotracheal Intubation

Table 4.2 shows the distribution of defective teeth in the 40 intubated and 23 non-intubated children. To investigate the effects of endotracheal intubation, it is necessary only to study the dental defects present in the upper incisors and canines as neither the laryngoscope nor the orotracheal tube would extend beyond the region of the maxillary canines.

Table 4.3 shows the frequency of defective maxillary anterior teeth in the intubated and non-intubated children. Thirty-four (85%) out of a total of 40 children in the intubated group had defects of the maxillary anterior teeth. These 34 affected children had a total of 56 defective maxillary anterior teeth. In the non-intubated group, only five (21.7%) out of a total of 23 children had defective maxillary anterior teeth. These five children had a total of 19 defective maxillary anterior teeth. This difference in the percentage of children affected in the two groups (85% versus 21.7%) is statistically significant ($\chi^2 = 24.46$, $p<0.001$, $df=1$). In contrast, no statistical difference is found in the mandibular anterior teeth between the intubated and non-intubated groups ($\chi^2 = 0.18$, $p>0.1$, $df=1$) indicating that the maxillary anterior teeth are being selectively affected (Table 4.3).

TABLE 4.2. The distribution of defective teeth in 40 intubated and 23 non-intubated very-low-birth-weight children.

	INTUBATED GROUP																					
	NUMBER OF DEFECTIVE MAXILLARY TEETH											NUMBER OF DEFECTIVE MANDIBULAR TEETH										
	Right					Left					Total	Right					Left					Total
Tooth	E	D	C	B	A	A	B	C	D	E		E	D	C	B	A	A	B	C	D	E	
Hypoplasia	0	0	3	3	4	15	10	3	2	1	41	1	0	4	0	1	1	0	6	1	0	14
Opacity	5	3	3	3	3	2	4	3	3	1	30	4	8	3	2	1	1	2	3	9	7	40
TOTAL	5	3	6	6	7	17	14	6	5	2	71	5	8	7	2	2	2	2	9	10	7	54

	NON-INTUBATED GROUP																					
	NUMBER OF DEFECTIVE MAXILLARY TEETH											NUMBER OF DEFECTIVE MANDIBULAR TEETH										
	Right					Left					Total	Right					Left					Total
Tooth	E	D	C	B	A	A	B	C	D	E		E	D	C	B	A	A	B	C	D	E	
Hypoplasia	0	2	0	1	3	4	2	0	1	0	13	0	2	0	1	0	0	1	0	1	0	5
Opacity	2	2	1	2	3	1	1	1	1	1	15	2	1	1	1	0	0	1	1	0	3	10
TOTAL	2	4	1	3	6	5	3	1	2	1	28	2	3	1	2	0	0	2	1	1	3	15

TABLE 4.3. Group characteristics of intubated and non-intubated children.

	Intubated Group (40 Children)	Non-intubated Group (23 Children)	p value
No. of children with defective maxillary anterior teeth (%)	34(85%)	5(21.7%)	<0.001 (χ^2=24.46) df = 1
No. of children with defective mandibular anterior teeth (%)	10(25.0%)	5(21.7%)	>0.1 (χ^2=0.18) df = 1
Gestational Age in weeks (mean ± S.D.)	29.0 ± 2.7	30.3 ± 1.9	>0.1 (t=1.17)
Birth Weight in gms (mean ± S.D.)	1088.3 ± 257.9	1269.1 ± 194.3	<0.05 (t=2.53)

Although the intubated group is comparable in gestational age to the non-intubated group (χ^2 = 1.17, p>0.1, df=1) they are approximately 200g smaller in terms of birth weight (t = 2.53, p<0.05), which indicates that both general and local factors may be operative in causing defective amelogenesis in the intubated group (Table 4.3). However, low birth weight does not seem to predispose to an increase in prevalence of dental defects in the whole group of 63 children. As can be observed in Table 4.4, there is no statistical difference in prevalence of defective dentition between children with birth weights less than 1000g and those 1000g and more (χ^2 = 0.91, p>0.1, df=1).

4.3.3 Effect of Laryngoscopy

In order to determine whether the endotracheal tube per se is responsible for the selective distribution and dental defects in our study population, the data were analysed by two separate procedures.

Table 4.5 shows the relationship between the length of intubation and the prevalence of dental defects. Dental defects occurred in 66.7% of the group receiving intubation for less than one day (usually for less than two hours), compared with 74.2% in the group intubated for two to 64 days (χ^2 with Yates' correction = 0.28, p>0.1, df=1). These results suggest that laryngoscopy, rather than the endotracheal tube itself,

TABLE 4.4: Relationship of birth weight to prevalence of dental defects.

BIRTH WEIGHTS	NO. OF CHILDREN	NO. OF CHILDREN WITH DEFECTIVE TEETH*
605- 999 gms	16	14 (87.5%)
1000-1500gms	47	37 (78.7%)

*$\chi^2 = 0.91$, $p>0.1$
(df = 1)

TABLE 4.5. Relationship of length of intubation to prevalence of dental defects.

Length of Intubation	Number of Children	
	Total	Defective maxillary anterior teeth (%) †
<1 day*	9	6 (66.7%)
2 days and greater**	31	23 (74.2%)

* length of intubation usually less than 2 hours.

** length of intubation from 2 days to as long as 64 days.

† $\chi^2 = 0.28$, $p>0.1$, $(df=1)$

may be the more important cause of the selective distribution of dental defects in our sample.

Further support of this conclusion is provided by analysis of left-sided and right-sided distribution of the defects in the maxillary anterior teeth, because in very-low-birth-weight infants, the laryngoscope is usually applied to the left-side of the midline. Table 4.6 shows the distribution of 56 defective maxillary anterior teeth on the right and left sides of the 34 intubated children with dental defects. Of great interest is the fact that in this group, the number of defective maxillary anterior teeth on the left side is twice as many as that on the right (66.1% versus 33.9%). This difference is statistically significant ($\chi^2 = 7.76$, $p<0.01$, $df=1$). By contrast, in the non-intubated group, no statistical difference is found between the numbers of defective anterior teeth on the left and right sides (47.4% versus 52.6%).

Table 4.2 indicates that in the intubated group, the maxillary left central and lateral incisors are by far the most commonly affected teeth. Also, hypoplasia is the common defect seen in these teeth. Figures 4.3 to 4.7 show the appearance of such typically affected maxillary left incisor teeth in intubated children.

TABLE 4.6. The left-sided and right-sided distribution of defective maxillary anterior teeth in intubated and non-intubated children.

	Total No. of maxillary anterior teeth per side (A B C)	Number of defective maxillary anterior teeth		p value
		Left side	Right side	
Intubated	102 (34 children)	37 (66.1%)	19 (33.9%)	<0.01 (χ^2=7.96) df = 1
Non-intubated	15 (5 children)*	9 (47.4%)	10 (52.6%)	>0.1 (χ^2=0.29) df = 1

* See Table 4.3

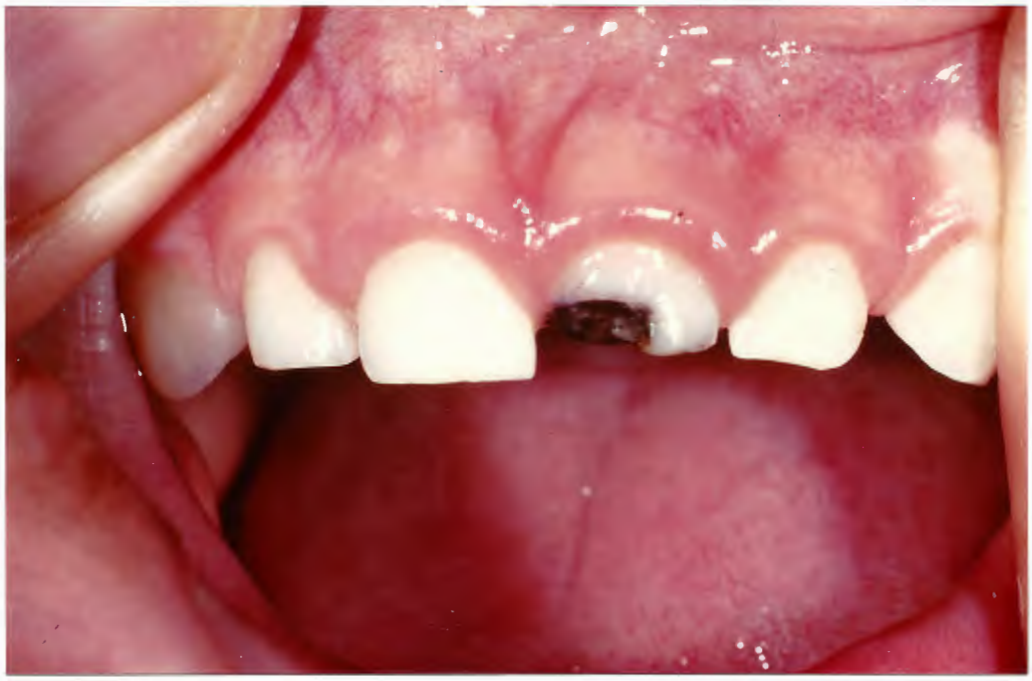


Figure 4.3 Hypoplastic left maxillary deciduous central incisor in a prematurely born, very-low-birth-weight child who was intubated during the neonatal period.

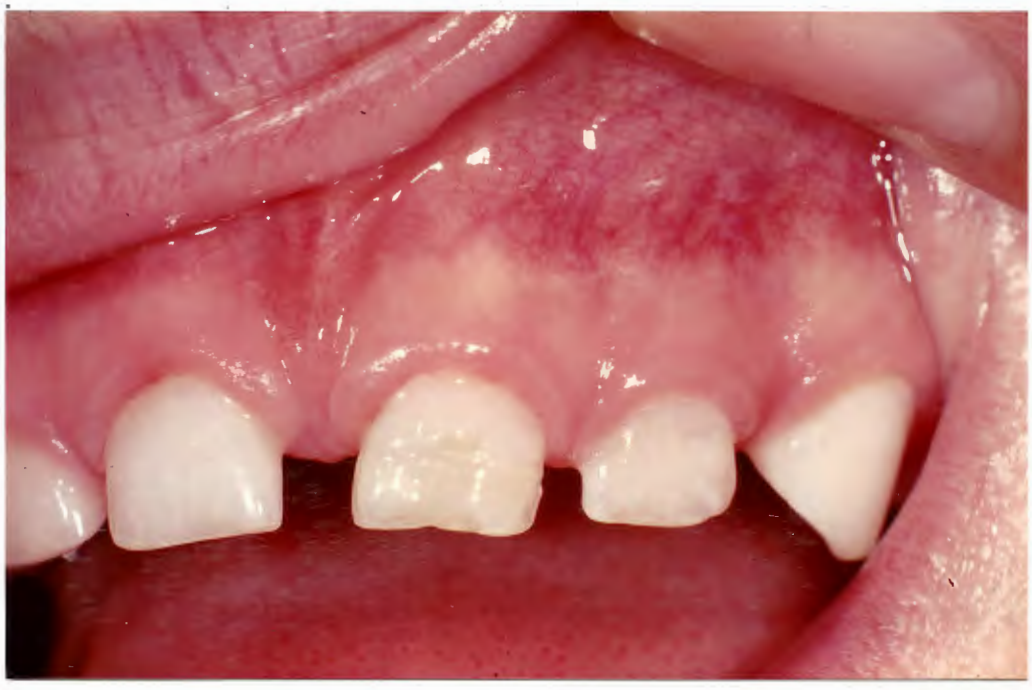


Figure 4.4 Defective left maxillary deciduous central incisor in a four year old girl who was intubated at birth for respiratory distress resulting from birth prematurity.

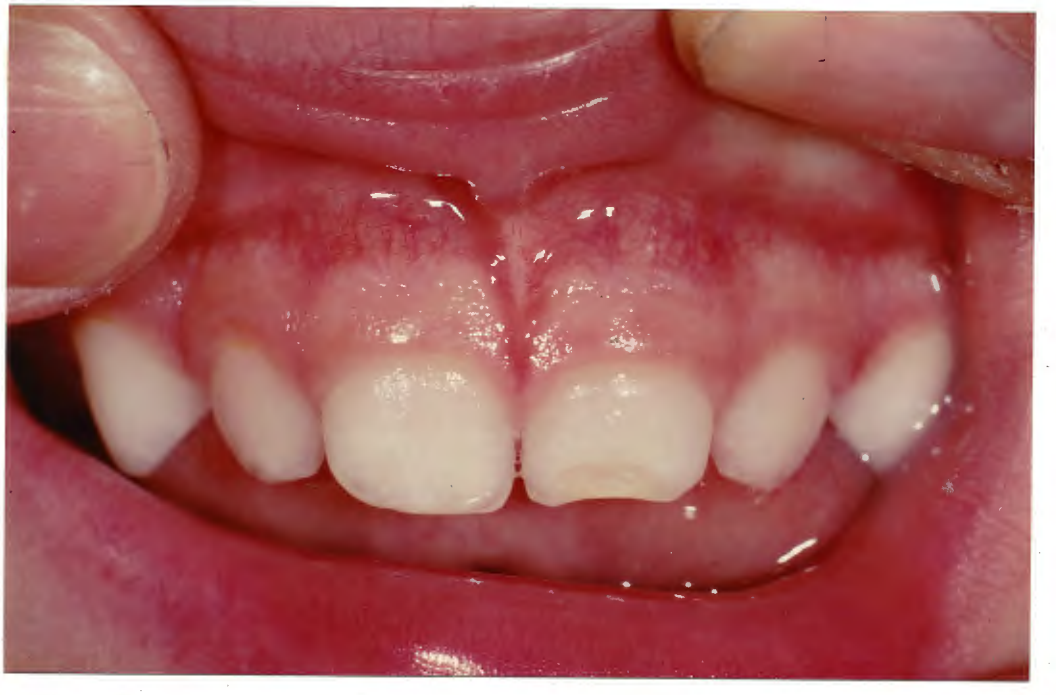


Figure 4.5 Hypoplasia of the left maxillary deciduous central incisor in an intubated two year old girl who was prematurely born with very low birth weight.

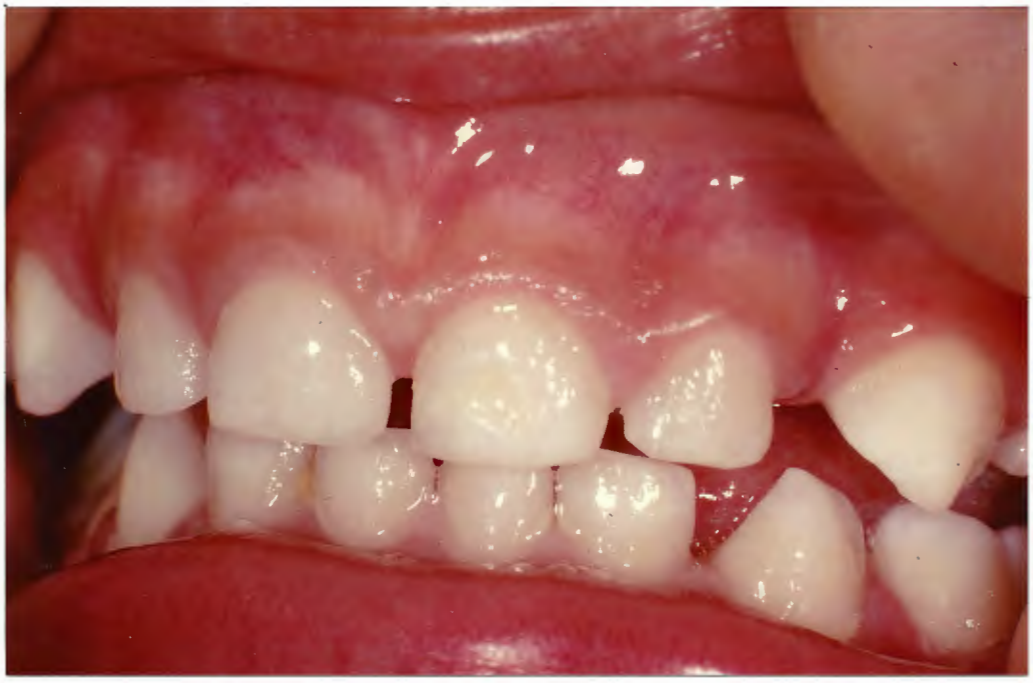


Figure 4.6 The anterior teeth of a three year-old boy who was prematurely born and intubated in the neonatal period. The left maxillary deciduous central incisor shows a depression in the centre of the labial surface of the crown.

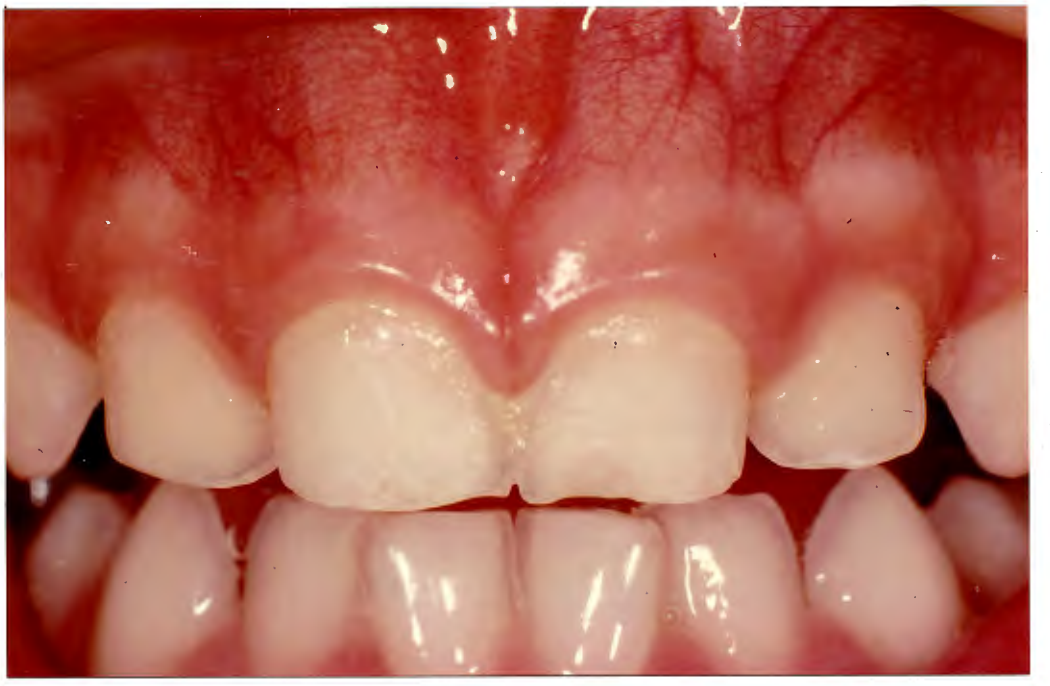


Figure 4.7 Hypoplasia of the left maxillary deciduous central incisor of a three year old girl who was prematurely born with very low birth weight and intubated in the neonatal period.

4.4 Discussion

The present study indicates that 79.4% of this group of 63 very-low-birth-weight children had developmental defects in the primary dentition, either in the form of opacities or enamel hypoplasia of the grown. Opacities, which are considered to be the result of influences during enamel maturation, were seen in 23.8% of the children. The more serious finding of enamel hypoplasia, which is thought to be due to earlier influences on enamel matrix formation, was detected in 55.6% of the children.

4.4.1 Systemic Factors

The frequency of dental defects in our study is much higher than that reported in previous studies on premature infants probably because of the lower birth weights in our sample. As early as 1947, Stein reported that prematurity was associated with an increased frequency of enamel hypoplasia. Grahnen and Larsson in 1958 reported that dental hypoplasia was present in 21% of premature infants compared with 2% in a control group. In 1962, Rosenzweig reported that 23.8% of prematurely born infants exhibited enamel hypoplasia. More recently, Funakoshi, et al., (1981) reported a frequency of 26.9% in a group of premature Japanese children, while Mellander, et al.,(1982) noted 17.5% in his sample of premature Swedish children.

This higher prevalence of dental defects found in our study can be attributed to the much lower birth weights of the children in our study. All our subjects had birth weights of less than 1500g whereas most previous studies included children of up to 2500g (Stein, 1947; Grahnen & Larsson, 1958; Rosenzweig & Sahar, 1962; Funakoshi, et al., 1981). It is well recognised that children of very low birth weights suffer greater complications in the neonatal period. One major problem is a disturbance in calcium metabolism, commonly seen in all premature infants but especially pronounced in those with very low birth weights (Tsang, et al., 1977). As amelogenesis is dependent on normal calcium metabolism, it is reasonable to suggest that it is the disturbed calcium metabolism present in premature infants that is the major factor involved in the pathogenesis and prevalence of dental defects in these children.

This hypothesis is supported by the findings in Chapte Three on a group of premature infants with a definitive diagnosis of rickets, which is a major disturbance in calcium metabolism. All the children in that study had developmental dental defects. Further support of this hypothesis comes from the observation that even full term infants with hypocalcaemic tetany, a relatively minor and transitory disturbance in calcium metabolism, have been shown to develop dental hypoplasia (Stimmler, et al., 1973; Purvis, et al., 1973).

The major aetiological factor causing the disturbance of calcium metabolism is still uncertain. It is known that two-thirds of the newborn's stores of calcium and phosphorus are accumulated in the third trimester of pregnancy (Tsang, et al., 1977). A premature infant born prior to this would have missed these accumulations. In addition, liver immaturity leading to defective vitamin D hydroxylation (Hillman, 1975), nutritional imbalances (Greer & Steichen, 1982) and hormonal factors (Root, 1976) may also be involved. Gastrointestinal diseases may also interfere with the absorption of calcium, phosphorus and vitamin D.

In an attempt to overcome this calcium imbalance, all the infants in our study received vitamin D 450 i.u. per day and calcium gluconate 300mg/kg/day supplements to their basic feeds of expressed breast milk or milk formula. In spite of this, the prevalence of dental defects remained very high in this group of children.

4.4.2 Local Factors

The present study also indicates that the adverse influences of systemic factors on amelogenesis may be compounded by local traumatic factors, the most obvious being laryngoscopy and orotracheal intubation. In support of this reasoning is the observation that, in the intubated group of children, the distribution

of the defective dentition is selectively localised to the region of the upper anterior teeth, notably the left central and lateral incisors. This distribution can be better explained by the traumatic effects of laryngoscopy rather than by orotracheal intubation for the following reasons. Firstly, the orotracheal tube is routinely taped to the midline, and with regular turning of the infant, it should be displaced evenly on both sides of the midline, rather than predominantly on the left. Secondly, the prevalence of dental defects did not correlate with the duration of orotracheal intubation. Thirdly, it has previously been reported that traumatic damage to erupted upper anterior teeth can be inflicted by laryngoscope leverage (Wasmuth, 1960).

In the neonate the process of laryngoscopy involves insertion of the laryngoscope blade into the right side of the mouth, but the handle has to be brought across just to the left of the midline in order to create enough room for the insertion of the orotracheal tube. The instrument is so constructed that it is always held with the left hand, while the right hand is occupied with insertion of the orotracheal tube along the groove, which is on the right side of the laryngoscope blade. Ideally, no force should be applied to the maxilla during the process of laryngoscopy. However, in very small infants, especially those of very low birth weight, the mandible

is so hypoplastic and underdeveloped that it does not provide a sufficient fulcrum for lifting the anterior oropharynx and tongue in order to expose the laryngeal opening. Thus an inadvertent leverage force is sometimes exerted on the maxillary anterior alveolar ridge, on the left side adjacent to the midline. Figure 4.8 depicts the intubation process.

The importance of the orotracheal tube cannot be discounted completely as another possible local cause of dental defects. Boice, et al., (1976) reported a non-surviving low-birth-weight infant who showed a notable concavity of the anterior left maxillary ridge clearly outlining the placement of the orotracheal tube. Sections taken through the notched alveolar ridge showed severe disruption of the developing enamel organ. Other workers (Krous, 1980; Wetzel, 1980) too have observed the development of an indentation on the anterior ridge of mechanically ventilated infants due to continual trauma from orotracheal tubes.

4.5 Conclusions

In this series of 63 children who had very low birth weights, it was found that 55.6% had enamel hypoplasia and 23.8% had dental opacities, giving a

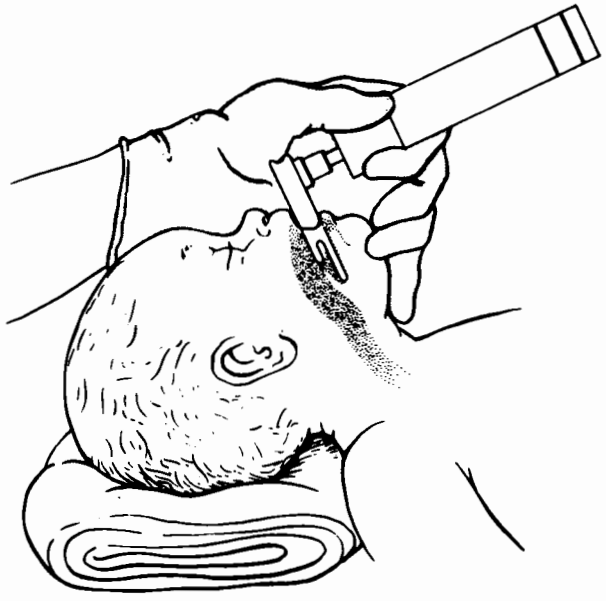


Figure 4.8 Diagram showing the intubation process in a neonate. Note that the laryngoscope is held with the left hand so that the endotracheal tube can be inserted with the right hand along the groove which is on the right side of the laryngoscope blade. The handle of the laryngoscope has to be brought just to the left of the midline in order to create enough room for the insertion of the endotracheal tube. Thus any leverage force exerted on the maxillary alveolar ridge will be in the region of the left maxillary central and lateral incisors.

very high prevalence rate of 79.4% with developmental defects in the primary dentition. This prevalence was much higher than those reported in previous studies of higher mean birth weights, and was probably due to the greater derangement of calcium metabolism in the neonatal period in very-low-birth-weight infants at a critical period of amelogenesis.

The selective distribution of dental defects in intubated infants to the left maxillary anterior teeth indicates that traumatic injuries produced by laryngoscopy and orotracheal intubation may further compound the already high predisposition of very-low-birth-weight infants to developmental defects in their primary dentition.

CHAPTER FIVE

EFFECT OF NEONATAL LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION ON PALATAL SYMMETRY IN TWO-TO-FIVE YEAR-OLD CHILDREN

5.1 Introduction

Laryngoscopy and endotracheal intubation often arerequired in the neonatal period for prematurely born, very-low-birth-weight infants to manage respiratory distress. However, complications can arise from this procedure, many of which are traumatic in origin. These include laryngeal oedema and tracheitis (Jordan, et al., 1970) and tracheal stenosis (Fishman, 1969). An important oral complication includes notching of the alveolar ridge caused by continual trauma of the tube abutting against it (Boice, et al., 1976; Wetzel, 1980; Krous, 1980). In addition, hypoplasia of the maxillary anterior teeth has been reported (Moylan, et al., 1980). Recently, Nowak and Erenberg (1982) found that 61 percent of low-birth-weight, intubated premature infants had either a palatal or alveolar ridge groove when examined at about 23 days after birth. Thus, it is established that

endotracheal intubation has a potential to alter palatal configuration in the neonatal period. However, no long term studies have been done to determine whether such alterations of palatal shape are persistent. This study examined palatal and dental arch symmetry in a group of two-to-five year-old, very-low-birth-weight children who were born prematurely and intubated in the neonatal period, to determine the effects of laryngoscopy and endotracheal intubation on palatal and arch symmetry.

5.2 Patients and Methods

5.2.1. Patients

The patients in this study were children attending the Growth and Development Clinic of the Mater Children's Hospital, South Brisbane. This clinic, which was established in 1978, provides a multidisciplinary follow up of all surviving infants of low birth weights managed at the Mater Mother's Hospital,

Of 63 children who were available for study, palatal impressions were obtained from 49 of them. These children were all prematurely born, with birth weights of between 605g and 1500g (mean 1213g). There

were 23 males and 26 females. Eighteen received endotracheal intubation and mechanical ventilation in the neonatal period, while 31 did not. At the time of dental examination the ages of the children ranged from two years two months to five years five months (mean three years three months). None of the patients in this study had any neurological abnormalities or facial dysmorphology, one child with cleft palate having been excluded. In addition, a history of constant thumb or finger sucking up to a year prior to the dental examination excluded a patient from the study. Also, no children in the study had undergone further episodes of intubation since leaving the hospital after birth.

5.2.2 Clinical examination and impression taking

The dental examinations were performed under ideal conditions at the University of Queensland Dental School. Obvious palatal defects such as grooves, as well as dental defects were recorded in a comprehensive chart. Intra-oral photographs were taken in some children. Postnatal medical and dental histories were obtained from the parents. Maternal and neonatal medical histories were obtained from hospital records.

A compound maxillary impression supported on a plastic spoon was taken of each patient (Figure 5.1).

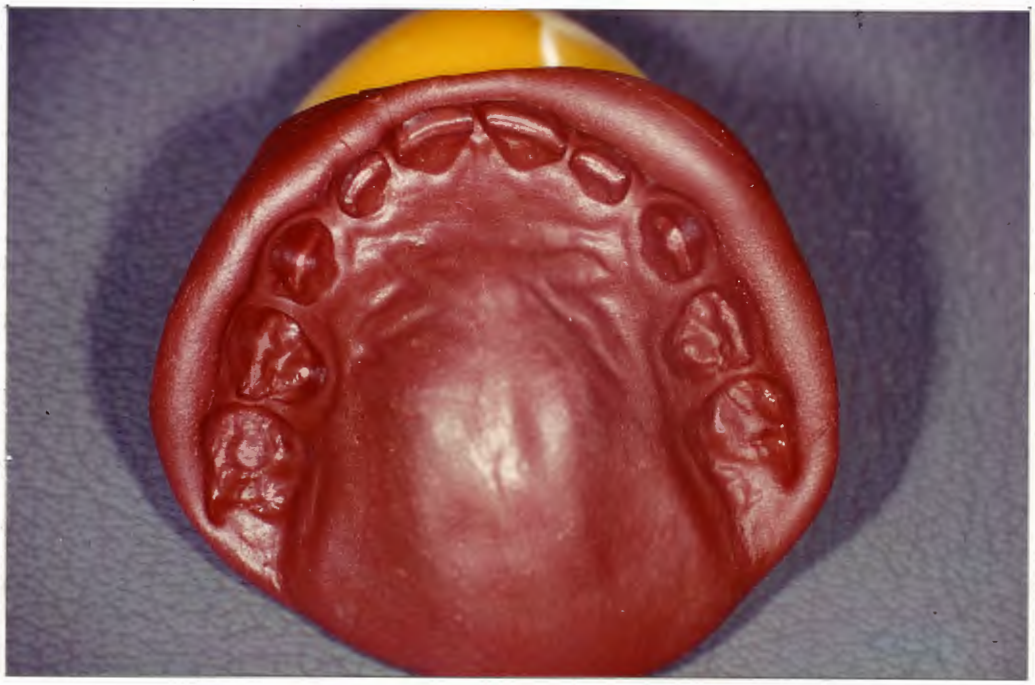


Figure 5.1 Compound impression taken from a three year old boy. The impression was supported on a yellow spoon.

Stone models were later formed from these impressions.

5.2.3 Measurement of palatal symmetry

Palatal asymmetry can be expected to be accompanied by arch asymmetry. In addition, as trauma from the laryngoscope and orotracheal tube is observed mainly in the alveolar part of the palate, any palatal distortion would manifest primarily as arch distortion. Arch asymmetry can be measured by comparing the location of corresponding selected reference points on a pair of contralateral teeth. The spatial location of the reference point on each tooth can be determined by the values of x, y and z coordinates of the Cartesian scale, with reference to a particular fixed plane (Figure 5.2). Comparison of the coordinates of the reference point on a tooth with that of the tooth on the other side of the arch will show discrepancies of the arch form in these dimensions, i.e. the horizontal (x coordinate), vertical (y coordinate) and depth (z coordinate).

The teeth at which measurements were taken were the deciduous lateral incisors, canines and first molars. As not every patient in the study had their second deciduous molars erupted, measurements were not taken at these teeth. The reference point on each tooth on the model was located on the gingival margin by drawing tangents to the mesio-palatal and disto-palatal surfaces

Figure 5.2 Photograph of a model mounted on an adjustable stand in preparation for measurements to be taken on the Olivetti Inspector machine.
The x, y z axes of the Cartesian coordinate system have been drawn in the photograph, to depict the relationship of the reference points to these axes.

and projecting a line bisecting the angle of their intersection to the gingival margin. These reference points were marked on the model. In addition, the median palatal raphe was also marked, and was used as a reference line to determine symmetry of the palate and dental arch in the horizontal dimension. As there are no absolute reference points, it is combined palatal and dental arch symmetry which is assessed by these measurements, hereafter called palatal and arch symmetry.

As shown in Figure 5.3, the reference points on the right deciduous lateral incisor is designated B_1 and that on the left incisor is B_2. The point on the median raphe on the same x axis as B_1 is designated B_4 and that on the same x axis as B_2 is B_3. Thus the x coordinate of B_4 (x_{B_4}) minus the x coordinate of B_1 (x_{B_1}) will give the width of B_1 to the midline raphe. Similarly x_{B_2} minus x_{B_3} will give the width of B_2 to the midline raphe. The difference of these two widths measures palatal asymmetry in the horizontal direction at the two reference points.

Similarly, the difference in the y coordinates of B_1 and B_2 measures palatal and arch asymmetry in the vertical direction; the difference in the z coordinates measures palatal asymmetry in the direction of depth. The horizontal reference plane for the z measurements was that defined by D_1, D_2 and the incisive papilla.

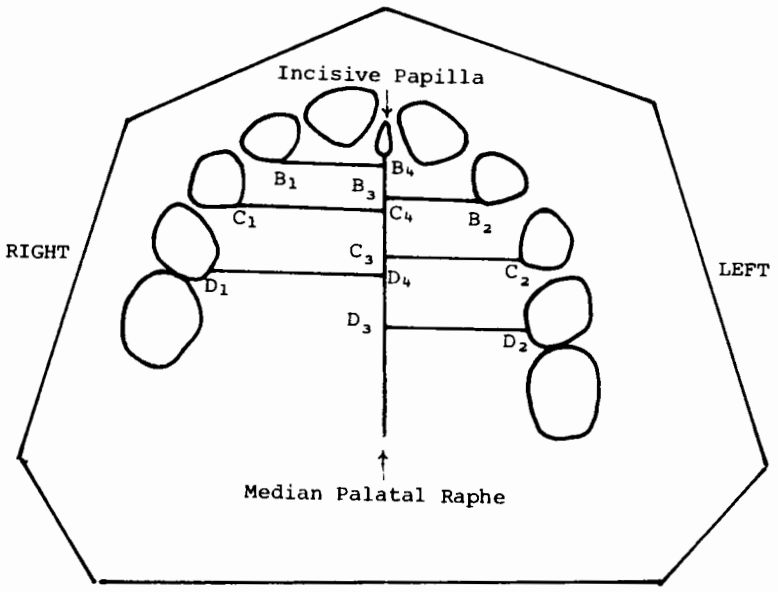


Figure 5.3 Diagrammatic representation of a maxillary dental cast used in the study. Reference points on the deciduous lateral incisor, canine and first molars are shown. These reference points were obtained by drawing tangents to the mesiopalatal and distopalatal surfaces and a line bissecting the angle between the tangents is projected to the gingival margin of each tooth.

Note that the reference point on the right deciduous lateral incisor is designated B_1 and that on the left incisor is B_2. Reference points on other teeth are designated accordingly. The point on the median palatal raphe at the same x axis as B_1 is designated B_4 and that on the median palatal raphe at the same x axis as B_2 is designated B_3. Corresponding points on other teeth are numbered accordingly.

Reference points on the other teeth were numbered correspondingly and similar determinations of differences at the various locations were computed.

The data were analysed using the student's t test to detect statistical differences between the groups.

5.2.4 Machine used for measuring palatal dimensions

The x, y and z coordinates of each reference point on a tooth can be determined directly using the Olivetti Inspector machine, located at the Telecom Workshop at Bulimba, Queensland. This equipment is an advanced measuring device which permits fast and accurate measurement of dimensions and marking out of production pieces in engineering. Figure 5.4 shows the diagrammatic representation of the machine and its various features. Essentially it allows direct measurement of dimensions on the three Cartesian axes on a millimetre scale with high accuracy. For this study, measurements were taken to the nearest tenth of a millimetre. The measurements are read directly on a display panel. In addition, the machine allows for the possibility of resetting each axis in any point of the travel, and locking on each of the three axes is possible.

The machine calibration was checked against a millimetre scale for each of the three axes prior to taking any measurements.

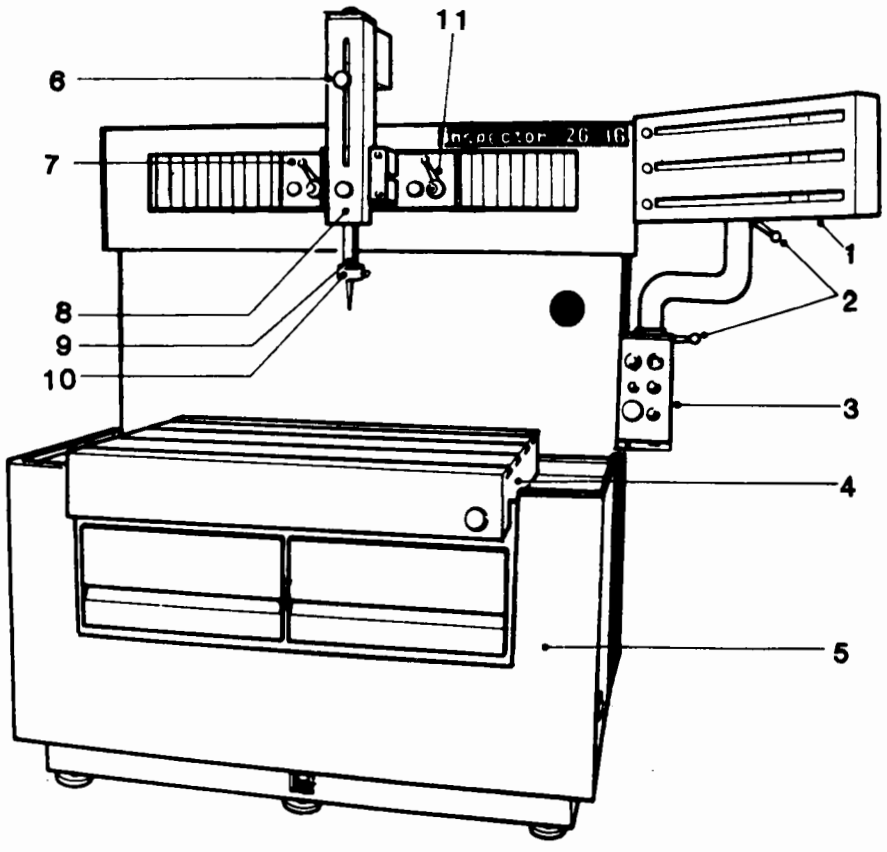


Figure 5.4 The Olivetti Inspector machine used for palatal measurements.

Key

1. Display of measurements in x, y, z coordinates
2. Locks for display unit
3. Switch on panel
4. Worktable
5. Electronic processing unit
6. Lock for z axis
7. Lock for x axis
8. x axis unit
9. z axis quill
10. Hand grip
11. Lock for y axis

Before measurements were taken of a model, it was first mounted on a stand with an adjustable table. The points D_1, D_4 and the centre of the incisive papilla were made co-planar and all measurements were made relative to this plane.

5.2.5 Validation of method

To determine the accuracy of the impression method and of the measurements of the palate, a preliminary experiment was performed. Three patients (aged three years two months, three years one month and four years five months) not forming part of the study population but attending the student paediatric dentistry clinic at the University of Queensland, had maxillary compound impressions taken, employing a technique identical to that used in the study. Two impressions were taken from each of these three patients and each stone model was measured three times.

Table 5.1 shows the results of the preliminary experiment. The accuracy of the measuring technique was shown by the small standard deviation (0.1 to 0.4mm) of three measurements taken of any one model.

In addition, the reproducibility of the impression and model-forming methods was established as follows. The mean differences between the left and

Table 5.1 Measurement of palatal symmetry in patients in preliminary experiment: Validation of method.

Model	Reference Teeth	Mean difference (mm ± S.D. of 3 measurements) between reference points on the contralateral teeth indicated, taken at each Cartesian axis of reference.		
		x	y	z
Patient No. 1				
First model	D | D	1.2 ± 0.3*	0†	0†
Second model		1.2 ± 0.1	0†	0†
First model	C | C	0.6 ± 0.2	0.2 ± 0.1	0.2 ± 0.2
Second model		0.6 ± 0.3	0.6 ± 0.3	0.2 ± 0.1
First model	B | B	0.6 ± 0.2	0.4 ± 0.1	0.1 ± 0.1
Second model		0.4 ± 0.2	0.3 ± 0.2	0.1 ± 0.1
Patient No. 2				
First model	D | D	1.1 ± 0.2	0†	0†
Second model		1.1 ± 0.4	0†	0†
First model	C | C	0.3 ± 0.1	0.1 ± 0.1	0.1 ± 0.1
Second model		0.6 ± 0.3	0.1 ± 0.1	0.1 ± 0.1
First model	B | B	0.3 ± 0.3	0.3 ± 0.2	0.1 ± 0.1
Second model		0.3 ± 0.1	0.2 ± 0.1	0.3 ± 0.2
Patient No. 3				
First model	D | D	1.5 ± 0.2	0†	0†
Second model		1.2 ± 0.2	0†	0†
First model	C | C	0.7 ± 0.3	0.3 ± 0.3	0.3 ± 0.1
Second model		0.5 ± 0.4	0.4 ± 0.2	0.2 ± 0.2
First model	B | B	0.5 ± 0.4	0.3 ± 0.2	0.2 ± 0.2
Second model		0.6 ± 0.4	0.3 ± 0.2	0.3 ± 0.1

* The standard deviation indicates the degree of measurement error of the three measurements taken of each model.

† Set to zero to provide a reference point for other measurements.

Comparison between the 2 models from any one patient showed no statistical difference with regard to each Cartesian axis of reference.

right reference points on each model were compared with those of another model taken from the same patient. These differences measure the symmetry of the palate and arch of each model at the various reference points. As shown in Table 5.1, comparison of these measurements of symmetry of the two models taken from each patient showed no statistical differences between models ($p>0.1$). This was true for all measurements taken at all Cartesian axes of references.

5.3 Results

Of the 31 children who were intubated during the neonatal period, no palatal grooves were observed on clinical examination.

Table 5.2 shows the measurements of palatal and arch symmetry in the intubated and non-intubated groups of children. As determined by the Student's t test, it is evident that there are no significant differences between the location of a reference point on a tooth on the right side compared with that on the tooth on the left. These reference points showed no significant differences in all three Cartesian axes (i.e. x, y, z) indicating that the palate and arch are symmetrical at all these reference points ($p>0.1$). The possibility that positive palatal asymmetry could be compensated

Table 5.2 Measurements of palatal symmetry in 31 intubated and 18 non intubated children.

Group	Reference Teeth	Mean difference (mm±S.D.) of reference points on the contralateral teeth indicated, taken at each Cartesian axis of reference.		
		x	y	z
Intubated	D | D	0.9 ± 0.7	0*	0*
Non Intubated		0.7 ± 0.5	0*	0*
Intubated	C | C	0.8 ± 0.7	0.5 ± 0.4	0.2 ± 0.1
Non Intubated		0.7 ± 0.5	0.5 ± 0.4	0.3 ± 0.2
Intubated	B | B	0.4 ± 0.3	0.4 ± 0.2	0.2 ± 0.2
Non Intubated		0.5 ± 0.4	0.4 ± 0.3	0.2 ± 0.2

The difference between intubated and non intubated children were non significant at all the reference points, in all 3 dimensions. ($p > 0.1$).

* set to zero.

for by complementary negative arch asymmetry is highly unlikely, since the forces tending to produce both act in the same direction.

To examine the possible effects of the length of intubation on palatal and arch symmetry, the palatal measurements of a group of 13 children who were intubated for three to ten days were compared with nine children who were intubated for greater than 20 days. As can be seen in Table 5.3, there were no significant differences in the measurements between these two groups ($p>0.1$), indicating that the length of intubation does not effect palatal symmetry.

The group of eight children who had endotracheal intubation for less than a day would have been subjected to the effects of the laryngoscope but would have had minimal effects of the endotracheal tube. Comparison between this group and the non-intubated group again showed no statistical difference in the measurements of palatal symmetry ($p>0.1$) (Table 5.4), showing that limited used of the laryngoscope alone is not likely to affect palatal and arch symmetry.

The standard deviations of the measurements in most study groups are larger than those of the measurements in the preliminary validation of data experiment.

Table 5.3 Effect of length of intubation on palatal symmetry.

Group*	Reference Teeth	Mean difference (mm±S.D.) of reference points on the contralateral teeth indicated, taken at each Cartesian axis of reference.		
		x	y	z
Group 1	D | D	0.9 ± 0.5	0	0
Group 2		0.9 ± 0.6	0	0
Group 1	C | C	0.8 ± 0.8	0.6 ± 0.4	0.3 ± 0.2
Group 2		0.5 ± 0.5	0.6 ± 0.5	0.4 ± 0.2
Group 1	B | B	0.4 ± 0.3	0.5 ± 0.3	0.2 ± 0.2
Group 2		0.4 ± 0.4	0.3 ± 0.3	0.3 ± 0.2

The differences between the groups were non significant at all the reference points in all 3 dimensions ($p > 0.1$).

*Group 1 (n=13) were intubated for 3-10 days.
Group 2 (n=9) were intubated for 20-64 days.

Table 5.4 Effect of very short term intubation (<1 day) on palatal symmetry.

Group	Reference Teeth	Mean difference (mm±S.D.) of reference points on the contralateral teeth indicated, taken at each Cartesian axis of reference.		
		x	y	z
Intubated for <1 day (n= 8)	D | D	0.9 ± 0.7	0	0
Non Intubated (n=18)		0.7 ± 0.5	0	0
Intubated for <1 day	C | C	1.0 ± 0.8	0.4 ± 0.3	0.2 ± 0.2
Non Intubated		0.7 ± 0.5	0.5 ± 0.4	0.2 ± 0.1
Intubated for <1 day	B | B	0.5 ± 0.4	0.3 ± 0.3	0.1 ± 0.1
Non Intubated		0.5 ± 0.4	0.4 ± 0.2	0

The differences between the groups were non significant at all the reference points in all 3 dimensions ($p > 0.1$).

This indicates that the potential does exist to detect differences in the measurements in the study groups, taking into account measurement errors. Therefore, such differences did not in fact exist, and palatal and arch symmetry between both groups of intubated and non-intubated children was demonstrated.

5.4 Discussion

Various types of equipment have been devised by researchers over the years to measure palates. Korkhaus (1930) invented the symmetrograph which transcribes actual palatal shape in two dimensions on to a piece of paper mounted vertically. Lebret (1962) used this method successfully to measure growth changes of the palate. Redman, et al., (1966) used a specially constructed device which can measure the height, width and depth of palates directly in the mouth. This device requires a lot of cooperation from the patient and would not be suitable for young children.

The measurement of dental casts using a three-dimensional co-ordinate system has been suggested by Van der Linden (1978) using a device called the Optocom. The Olivetti-Inspector machine used in this study measured the dental casts employing a similar principle. However, it is a more sophisticated machine and more

accurate. The technique of measurement using this machine is simple, and it is the most suitable and accurate of devices available to us for palatal measurements in young children.

The results of the preliminary experiment indicated that our method of impression-taking and model-pouring is accurate and reproducible. Impression-taking in two or three year old children requires skill in patient management and our technique of using compound supported on a plastic spoon appeared to be very well accepted by all patients in our study. Other authors (Lebret, 1962; Nowak & Erenberg, 1982) have also successfully used compound impressions to study palate shapes in children.

The fact that laryngoscopy and endotracheal intubation can have traumatic effects on the oral tissues in the neonatal period has been established. Boice, et al., (1976), Krous (1980), Wetzel (1980) as well as Nowak and Erenberg (1982) observed the development of grooves on the alveolar ridge and palate in infants who were intubated after birth. In addition, dilaceration of a developing incisor tooth germ reported in the study of Boice, et al., (1976) implicated a displacing force in the anterior alveolar region. This traumatic force could have resulted from either the laryngoscope or endotracheal

tube applied during the neonatal period. Hypoplasia of the teeth associated with laryngoscopy and endotracheal intubation (Moylan, et al., 1980) provides further proof of trauma resulting from these procedures.

However, although laryngoscopy and endotracheal intubation have a potential for causing palatal deformation, this study has shown that no palatal and arch asymmetry is evident in two-to-five year-old children intubated in the neonatal period. No significant differences were found in the measurements taken on the left and right sides in both intubated and non-intubated groups. In addition, the length of intubation does not appear to affect palatal symmetry.

Growth changes and remodelling of the palate and alveolus in the first few years of life probably correct any deformation of the palate caused by laryngoscopy and endotracheal intubation. That growth changes can allow for remodelling of the palate is seen in patients with thumb or finger sucking habits. Most cases of uncomplicated palatal deformities resulting from digit sucking are resolved once the habit is discontinued (Larsson, 1972).

In conclusion, this study has shown that no palatal or arch asymmetry is evident in two-to-five-year-old children who had neonatal laryngoscopy and

endotracheal intubation compared with a group of non-intubated children. This indicates that although laryngoscopy and endotracheal intubation have the potential to cause palatal and arch deformation, there are no persistent detrimental effects on these structures.

CHAPTER SIX

DISCUSSION

6.1 Introduction

In the previous chapters, clinical findings on the dentition of children born with very low birth weights as well as those who had neonatal rickets were presented. In addition, the palatal configurations of children who underwent intubation and mechanical ventilation in the neonatal period were assessed. This chapter discusses the findings of this study and attempts to place these observations in perspective in the light of previous work and a current hypothesis regarding the pathogenesis of enamel hypoplasia.

6.2 Prevalence of Enamel Hypoplasia in Primary Teeth

The prevalence of non-hereditary enamel hypoplasia in primary teeth in the general population in low fluoride areas ranges from about 3 percent in Scandinavian countries (Magnusson, 1981) to about 6 percent in England and Wales (Ainsworth, 1925). In Australia, the prevalence is estimated to be around 2 percent (Brown, 1975).

The frequency of enamel hypoplasia in the present study population of prematurely born, very-low-birth-weight children is 55.6 percent. An additional 23.8 percent had enamel opacities, giving a total of 79.4 percent of children with developmental enamel defects. This figure is extremely high compared with the prevalence in the general population.

Earlier studies on premature infants also reported an increased frequency of enamel defects. Stein (1947) found that eight out of 16 children born prematurely had enamel hypoplasia. Grahnen and Larsson (1958) reported that enamel hypoplasia was present in 21 percent of premature infants compared with two percent in a control group. In 1962, Rosenzweig and Sahar observed that 23.8 percent of prematurely-born infants exhibited enamel hypoplasia. More recently, Funakoshi, et al., (1981) found a frequency of 26.9 percent in a group of premature Japanese children, while Mellander, et al., (1982) noted 17.5 percent in his sample of premature Swedish children.

6.3 Hypothesis for the Aetiology of Enamel Hypoplasia in Premature Infants

Compared with the above previous reports, the present study showed a greater frequency of enamel defects. This can be attributed to the much lower birth

weights of the children in this study. All the subjects in this study had birth weights of less than 1500g, whereas most previous studies included children of up to 2500g. Infants of very low birth weights sustain more complications in the perinatal period; these systemic derangements may lead to greater disturbances of enamel formation.

The perinatal factors involved in the aetiology of enamel hypoplasia in the premature infant have not been clearly identified. Disturbances of calcium metabolism are now gaining increasing recognition as serious complications of many conditions encountered by premature infants in the neonatal period (Tsang, et al., 1973; Root & Harrison, 1976). As amelogenesis is dependent on normal calcium metabolism (Gaunt & Irving, 1941), it is reasonable to suggest that it is the disturbed calcium metabolism present in premature infants that is the major factor involved in the pathogenesis and prevalence of generalised dental defects in these children.

This hypothesis is strengthened by the findings in the group of children who had neonatal rickets, a major disturbance in calcium metabolism. All 15 children who developed neonatal rickets had defects in their primary teeth. Twelve (80%) children had hypoplasia and opacities of the teeth whereas three (20%) had opacities alone.

Further support for an important role of calcium metabolism in the pathogenesis of developmental dental defects is provided by dental observations of other conditions with disturbances in calcium homeostasis. Even in a relatively mild and transient type of hypocalcaemia such as neonatal tetany, enamel hypoplasia can result (Purvis, et al., 1973; Stimmler, et al., 1973). In more severe disturbances such as vitamin D deficiency rickets, enamel hypoplasia is frequently seen (Eliot, et al., 1934; Grahnen & Selander, 1954). Similar observations are noted in hereditary vitamin D-dependency rickets (Hall, 1959; Witkop, 1975) and in hypoparathyroidism (Pisanty & Garfunkel, 1977).

6.3.1 Major causes of calcium disturbances in premature infants

The major aetiological factor causing the disturbance of calcium metabolism in very-low-birth-weight premature infants is still uncertain. Two-thirds of the newborn's stores of calcium and phosphorus are accumulated during the third trimester of pregnancy (Tsang, et al., 1977) and a premature infant born prior to about 28 or 30 weeks' gestation would have missed much of this mineral accretion. Nearly all the children in this study were born prior to 28 weeks' gestation; thus they had low calcium and phosphate stores in the neonatal period.

Furthermore, at birth, when the umbilical cord is clamped, there is an abrupt cessation of the maternal supply of calcium and phosphate, leaving the infant to draw from its own stores of calcium and phosphate or to derive these minerals from exogenous sources in order to maintain adequate serum levels (Tsang, 1983). Even in a normal full-term infant, in the first few hours after the umbilical cord is clamped, hypocalcaemia is frequently encountered as the newborn attempts to adjust to the cessation of the maternal supply of calcium (Root & Harrison, 1976). Homeostasis is frequently achieved by increased activity of the parathyroid glands, and increased absorption of vitamin D and calcium from the gastro-intestinal tract.

However, in the very-low-birth-weight, premature infant, compensation for the cessation of maternal supply of mineral may not be adequately achieved due to the immaturity of the parathyroid glands (Tsang, 1973). In addition, liver and kidney immaturity may result in defective vitamin D metabolism (Seino, et al., 1981). Failure to supply adequate calcium and phosphate as well as poor intestinal absorption are also important factors (Tsang, 1983). Thus, the lack of exogenous supply of calcium and phosphate, together with inadequate stores of these minerals, accounts for the decreased mineralisation of the bones and teeth of these infants.

6.3.2 Other causes of calcium disturbances in premature infants

Various complications associated with prematurity further predispose the very-low-birth-weight infants to hypocalcaemia in the neonatal period. These are outlined in Table 6.1, and can occur in utero, at delivery or during the neonatal period.

Pregnancy complications known to decrease serum calcium concentrations in the neonatal period include maternal diabetes (Tsang, 1975), toxaemia (Tsang, 1973), hyperparathyroidism (Fanconi & Prader, 1967) and maternal deficiency of dietary calcium and vitamin D (Davis, et al., 1978). In these conditions, the causes of hypocalcaemia are not fully understood but are most likely to be related to malfunction of the parathyroid glands and inadequate supply of calcium to the foetus.

Traumatic delivery, e.g. Caesarean section and cerebral injuries, are also associated with neonatal hypocalcaemia (Root & Harrison, 1976). In addition, birth asphyxia is often complicated by hypocalcaemia (Tsang, 1973). In the newborn period, respiratory distress syndrome, sepsis and hyperbilirubinaemia also often result in hypocalcaemia (Tsang, et al., 1973). Again, the causes for the low calcium levels are related to stressed parathyroid glands which are unable to maintain serum calcium levels.

Table 6.1 Medical Complications Causing Hypocalcaemia in the Newborn

Time	Complication
In utero	Maternal diabetes mellitus
	Maternal toxaemia
	Maternal deficiency of dietary calcium, vitamin D
	Maternal hyperparathyroidism
	Placenta insufficiency
Delivery	Prematurity
	Traumatic delivery, e.g. Caesarean section
	Asphyxia
	Cerebral injuries
Neonatal	Hypoxia, e.g. respiratory distress syndrome
	Sepsis
	Hyperbilirubinaemia

Thus, the prematurely born, very-low-birth-weight infant can suffer serious derangements of calcium metabolism in the neonatal period, resulting not only from prematurity itself but also from various complications associated with prematurity. Therefore, it is not surprising that the prevalence of enamel hypoplasia is so high in the present study. Recent work by Noren *et al* (1984) has also supported the fact that hypocalcaemia is very common in prematurely-born children. Ground sections of deciduous teeth from these children revealed areas of hypomineralisation corresponding to the neonatal period; these areas of inadequate calcification were not seen in control teeth from children born full-term.

6.4 The Central Role of Calcium Disturbances in the Pathogenesis of Enamel Hypoplasia

The hypothesis that disturbances in calcium metabolism play a central role in the pathogenesis of enamel hypoplasia thus provides a unifying concept in the consideration of systemic causes of enamel hypoplasia in premature infants.

Extending this concept to full-term infants, it can be postulated that many systemic factors known to cause enamel hypoplasia in the primary dentition

actually do so by causing a disturbance in calcium metabolism. Even the neonatal line, which is a line of enamel hypoplasia seen microscopically in most normal teeth, can be explained by transient hypocalcaemia which occurs in all infants in the first few hours after birth as they attempt to compensate for the cessation of calcium supply from the mother.

Similarly, the hypoplasia seen in infants of diabetic mothers (Grahnen & Edlund, 1967) and those with a history of maternal toxaemia (Via & Churchill, 1959) may be attributed to the hypocalcaemia associated with these conditions. Also, the cause of the defective dentition observed in infants who suffered difficult births and cerebral injuries (Herman & McDonald, 1963; Perstein & Massler, 1956; Via & Churchill, 1959) as well as those who had birth asphyxia (Grahnen, et al., 1974) may be related to hypocalcaemia complicating these conditions.

It is, of course, possible that major metabolic insults can damage ameloblasts directly (Kreshover & Clough, 1953). However, in the premature, very-low-birth-weight infant, it is difficult to analyse the direct effect of metabolic factors on enamel hypoplasia because the underlying, confounding factor of calcium derangements, which is always present in these infants, cannot be separated.

6.5 Local Causes of Enamel Hypoplasia

The present study also indicates that the adverse influences of systemic factors on amelogenesis may be compounded by local traumatic factors, the most obvious being laryngoscopy and orotracheal intubation.

6.5.1 Laryngoscopy

The results of this study showed that enamel defects occurred in the maxillary anterior teeth of 85 percent of 40 intubated children compared with only 21.7 percent of non-intubated children, a fourfold difference. In addition, it was found that in the intubated group of children with defects of the maxillary anterior teeth, 66.1 percent of the affected teeth were on the left compared with 33.9 percent on the right, a twofold difference. This indicated that the left maxillary anterior teeth were selectively affected, a finding that can be explained by the position of the laryngoscope during the process of intubation. During this process, a leverage force may be exerted on the alveolar ridge on the left of the midline. Considering that the maxillary anterior teeth lie just beneath the mucosa, it is not surprising that amelogenesis can be readily disrupted by this leverage force. Also, it has been previously reported that the laryngoscope can traumatise maxillary anterior teeth in older children

and adults (Wasmuth, 1960; Bamforth, 1963; Powell & Keown, 1965).

6.5.2 Prolonged endotracheal intubation

The orotracheal tube is also another possible local cause of trauma to developing teeth. Boice, et al. (1976) have shown that severe disruption to an enamel organ can occur as a result of continual trauma to the alveolar ridge by an orotracheal tube placed in a low-birth-weight infant. Other workers (Krous, 1980; Wetzel, 1980) have reported that a groove develops on the anterior alveolar ridge of mechanically ventilated infants, and the orotracheal tubes have been observed to slot into these grooves once they have developed. Disturbances of enamel formation are expected to occur from such obvious trauma.

6.6 Effect of laryngoscopy and endotracheal intubation on palatal configuration

As trauma from the laryngoscope and endotracheal tube can cause dental defects, it is also possible that distortion and asymmetry of the palate can result from such forces. Many authors (Boice, et al., 1976; Krous, 1980; Wetzel, 1980) have observed the development of alveolar grooves in intubated infants in the neonatal

period. Recently, Nowak and Erenberg (1982) reported that 61% of low-birth-weight, intubated, premature infants had either a palatal or alveolar ridge groove when examined at about 23 days after birth. However, no previous long term studies have been done to determine whether such changes in palatal configuration are persistent.

This study has shown that no obvious palatal or alveolar grooves were observed in intubated children when examined at two-to-five years of age. In addition, measurements of the palate revealed no asymmetry of the palate or dental arch in the intubated group compared with the non-intubated group. In addition, the group of children who had been intubated for a prolonged period (20-64 days) did not have greater asymmetry of the palate than the group who were intubated for a comparatively short time (3-10 days). Thus, this study indicates that although laryngoscopy and endotracheal intubation have a potential for causing palatal deformation, no persistent detrimental effects are noted.

Growth changes and bone remodelling have probably removed any palatal deformations in the neonatal period. Unlike teeth which provide a permanent record of traumatic damage, bone is capable of remodelling and repairing any damage so that changes occurring in the neonatal period could have resolved by two-to-five years of age. Arch distortion due to digit sucking likewise resolves once the habit is stopped.

6.7 Conclusions

In conclusion, prematurely born, very-low-birth-weight children have a high predisposition to developmental defects in the primary dentition. The aetiology of this is multifactorial, the most important factor being calcium disturbances in the neonatal period. Contributory causes of enamel defects include trauma from laryngoscopy and endotracheal intubation. However, these local factors do not have persistent detrimental effects on palate and dental arch configuration.

BIBLIOGRAPHY

Aasenden, R. and Peebles, T.C. (1974). Effects of fluoride supplementation from birth on deciduous and permanent teeth. Arch. Oral Biol. 19:321-326.

Ackerman, B.D., Dyer, G.Y. and Leydorf, M.M. (1970). Hyperbilirubinaemia and kernicterus in small premature infants. Pediatrics 45:918-25.

Ainsworth, N.J. (1925). Incidence of dental diseases in children. Med. Res. Council Special Report Series No. 97, London: H.M. Stationery Office.

Albright, F. and Stock, M.S. (1933). Association of a calcification of dentin with hypoparathyroidism in rats and cure of same with parahormone with some correlated observations in man. J. Clin. Invest. 12:294-302.

Alexander, W.N. (1964). Composite dysplasia of a single tooth as a result of electric burn damage : report of case. J. Am. Dent. Assoc. 69:589-591.

Andreasen, J.O. and Ravn, J.J. (1971). The effect of traumatic injuries to primary teeth on their permanent successors. I. A clinical and histological study of 117 injured permanent teeth. Scand. J. dent. Res. 79:219-283.

Andreasen, J.O. and Ravn, J.J. (1973). Enamel changes in permanent teeth after trauma to their primary predecessors. Scand. J. dent. Res. 81:203-209.

Arander, J.V., Saheb, N., Stern, L. and Avery, M.E. (1971). Arterial oxygen tension and retinal vaso-constriction in newborn infants. Am. J. Dis. Child. 122:189-194.

Archard, H.O. (1971). The dental defects of vitamin D resistant rickets. Birth Defects : (original Article Series). VII:196.

Archard, H.O. and Witkop, C.J. (1966). Hereditary hypophosphataemia (vitamin D resistant rickets) presenting primary dental manifestations. Oral Surg. 22:184-193.

Axrup, K., D'Avignon, M. and Hellgren, K. (1966). Children with thalidomide embryopathy : odontological observations and aspects. Acta Odontol. Scand. 24:3-21.

Babeaux, W.L. and Zipkin, I. (1966). Dental aspects of the prenatal administration of fluoride. J. Oral Ther. Pharmacol. 3:124-135.

Baker, K.L. (1972). The fluorescent, microradiographic, microhardness and specific gravity properties of tetracycline-affected human enamel and dentine. Arch. Oral Biol. 17:525-536.

Bamforth, B.J. (1963). Complications during endotracheal anaesthesia. Anaesth. Analg. Curr. Res. 42:727-732.

Bauer, W.H. (1946). The effect of periapical processes of deciduous teeth on the buds of permanent teeth. Am. J. Orthod. 32:232-241.

Belanger, K., Sanger, R., Casamassimo, P.S. and Bystrom, E.B. (1982). Oral and systemic findings in biliary atresia : report of 11 cases. Pediatr. Dent. 4:322-326.

Belsey, R., Clark, M.B., Bernat, M., Glowacki, J., Holick, M.F., De Luca, H.F. and Potts, J.F. (1974). The physiologic significance of plasma transport of vitamin D and metabolites. Am. J. Med. 57:50-56.

Berger, E.N.H. (1978). Attitudes and preventive dental health behavior in children with congenital cardiac disease. Aust. Dent. J. 23:87-96.

Binstadt, D.H. and L'Heureux, P.R. (1978). Rickets as a complication of intravenous hyperalimentation in infants. Pediatr. Radiol. 7:211-214.

Black, G.V. and McKay, F. (1916). Mottled teeth. Dental Cosmos 58:129-156.

Boice, J.B., Krous, H.F. and Foley, J.N. (1976). Gingival and dental complications of orotracheal intubation. J. A. M. A. 236:957-958.

Boyle, I.T., Omdahl, J.L. and Gray, R.W. (1973). The biological activity and metabolism of 24,25 dihydroxyvitamin D_3. J. Biol. Chem. 248:4174-4180.

Bouyssou, M. (1962). Dysplasia of prenatal and neonatal deciduous teeth. Dent. Abs. 7:349-350.

Brauer, J.C. and Blackstone, C.H. (1941). Dental aspects of congenital syphilis. J. Amer. Dent. Assoc. 28:1633-1639.

Brooks, J.G. (1982). Respiratory tract and mediastinum. In Kemp, C.H., Silver, H.K. (eds) Current pediatric diagnosis and treatment. Los Altos: Lange Medical Publications, p. 28.

Brown, J.P. (1975). The epidemiology of tooth calcification defects and dental caries in Queensland children. Ph.D. thesis, University of Queensland.

Bunker, P.G. and Aberdeen, S.D. (1962). Dental factors in foreign body problems. Ann. Otol. 71:1973-2079.

Caffey, J. (1978). Pediatric X-ray diagnosis. Chicago: Year Book Medical Publishers, pp 1117-1118.

Cleghorn, G.J., Tudehope, D.I. and Masel, J.P. (1981). Rickets in extremely low birth weight infants. Aust. Paediatr. J. 17:285-289.

Cohn, R.M. and Roth, K.S. (1983). Metabolic Disease. Philadelphia: W. B. Saunders. pp 265-269.

Commission on Oral Health, Research and Epidemiology, F.D.I. (1982). An epidemiological index of dental enamel (DDE Index) Int. Dent. J. 32:159-167.

Cullen, S.C. (1961). Anaesthesia: a manual for students and physicians. Chicago: Year Book Publishers.

Davis, D.P., Hughes, C.A. and Moore, J.R. (1978). Rickets in preterm infants. Arch. Dis. Child. 53:88-90.

Dean, H.T. (1938). Endemic fluorosis and its relation to dental caries. Pub. Health Rep. 53:1443-1452.

De Luca, H.F. (1972). The functional metabolism of vitamin D_3. In Talmage, R.V. and Munson, P.L. (eds) Calcium, parathyroid hormone and the calcitonins. Amsterdam: Exerpta Medica, pp 221-225.

De Luca, H.F. (1975). The kidney as an endocrine organ involved in the function of vitamin D. Am. J. Med. 58:39-48.

De Wilde, H. (1943). Defective teeth in congenital syphilis. Amer. J. Ortho. 29:368-372.

Dixon, D.A. (1968). Defects of structure and formation of the teeth in persons with cleft palate and the effect of reparative surgery on the dental tissues. Oral Surg. 25:435-446.

Ecks, S., Gabrielson, L.H. and Halvorsen, S. (1957). Prematurity and rickets. Pediatrics 20:63-69.

Elliot, M.M., Souther, S.O., Anderson, B.G. and Arnim, S.S. (1934). A study of the teeth of a group of school children previously examined for rickets. Amer. J. Dis. Child. 48:713-720.

Evans, M.W. (1944). Congenital dental defects in infants subsequent to maternal rubella during pregnancy. Med. J. Aust. 31:225-228.

Evers, W., Racz, G.B., Glazer, J. and Dobkin, A.B. (1967). Orahesive as a protection for teeth during general anaesthesia and endoscopy. Can. Anaes. Soc. J. 14:123-128.

Ericsson, Y. and Ribelius, U. (1971). Wide variations of fluoride supply to infants and their effect. Caries Res. 5:78-88.

Fanconi, A. and Prader, A. (1974). Serum parathyroid hormone concentrations in hypophosphataemic vitam D resistant rickets. Helv. Pediatr. Acta, 29:187-194.

Faxelius, G., Raye, J., Gutbuler, R., Swanstrom, S., Tsiantos, A., Dolanski, E., Dehan, M., Dyer, N., Lindstrom, D., Brill, A.B. and Stahlman, M. (1977). Red cell volume measurements and acute blood loss in high risk newborn infants. J. Pediatr. 90:273-281.

Finerman, G.A.M. and Milch, R.A. (1963). In vitro binding of tetracyclines to calcium. Nature. 198:486-487.

Fishman, N. H. (1969). Post intubation tracheal stenosis. Ann. Thorac. Surg. 8:47-56.

Fiumara, N.J. and Lessell, S. (1969). Manifestations of late congenital syphilis. Arch. Dermatol. 102:78-81.

Flynn, C.J. and Lowe, A.R. (1973). Endotracheal tube swallowed by a neonate. Med. J. Aust. 1:62-63.

Forrester, R.M. and Miller, J. (1955). The dental changes associated with kernicterus. Arch. Dis. Child. 30:224-230.

Forsmann, B. (1974). Dental fluorosis and caries in high fluoride districts in Sweden. Comm. Dent. Oral Epidemiol. 2:132-148.

Forsmann, B. (1977). Early supply of fluoride and enamel fluorosis. Scand. J. dent. Res. 85:22-30.

Fraser, D. and Scriver, C.R. (1976). Familial forms of vitamin D-resistant rickets revisited: X-linked hypophosphataemia and autosomal recessive vitamin D dependency. Amer. J. Clin. Nutr. 29:1315-1323.

Fraser, D. and Nikiforuk, G. (1982). The aetiology of enamel hypoplasia in children - a unifying concept. J. Int. Ass. Dent. Child. 13:1-11.

Friedman, W.F., Hirschklau, M.J. and Pervitz, M.P. (1976). Pharmacologic closure of patent ductus arteriosus in the premature infant. N. Engl. J. Med. 295:526-529.

Funakoshi, Y., Kushida, Y., Hieda, T. (1981). Dental observations of low-birth-weight infants. Pediatr. Dent. 3:21-25.

Fyler, D.C. and Lang, P. (1981). Neonatal heart disease. In Avery, G.B. (ed.) Neonatalogy. Philadelphia: Lippincott, pp 438-472.

Gabbe, S.G. and Mestman, J.H. (1977). Management and outcome of pregnancy in diabetes mellitus. Am. J. Obstet. Gynecol. 127:465-469.

Gardner, D.E. and Prescott, G.H. (1969). Hereditary hypophosphataemia. J. Dent. Child. 36:199-216.

Gaunt, W.E. and Irving, J.P. (1941). The influence of dietary calcium and phosphorus upon tooth formation. J. physiol. 99:18-29.

Giro, C.M. (1947). Enamel hypoplasia in human teeth: an examination of its causes. J. Amer. Dent. Ass. 34:310-317.

Glorieux, F.H., Salle, B.L., Delvin, E.E. and David, L. (1981). Vitamin D metabolism in preterm infants: serum calcitriol values during the first five days of life. J. Pediatr. 99:640-643.

Grahnen, H. and Selander, P. (1954). The effects of rickets and spasmophilia on the permanent dentition. 1. The effect on the teeth. Odontol. Revy. 5:7-26.

Grahnen, H. (1958). Maternal rubella and dental defects. Odont. Revy. 9:181-192.

Grahnen, H. and Larsson, P.G. (1958). Enamel defects in the deciduous dentition of prematurely born children. Odont. Revy. 9:193-204.

Grahnen, H. and Granath, L. (1962). The effect of hyperbilirubinaemia on primary teeth. Odont. Revy. 13:337-343.

Grahnen, H. and Edlund, K. (1967). Maternal diabetes and changes in the hard tissues of primary teeth. I. A clinical study. Odont. Revy. 18:157-162.

Grahnen, H., Sjolin, S., Arwill, T. and Magnusson, B.D. (1969). Neonatal asphyxia and mineralisation defects of the primary teeth. Caries Res. 3:301-307.

Grahnen, H., Sjolin, S. and Stenstrom, A. (1974). Mineralisation defects of primary teeth in children. Scand. J. Dent. Res. 82:396-400.

Greer, F.R., Searcy, J.E., Levin, R.S., Steichen, J.J., Asche, P.S. and Tsang, R.C. (1981). Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D. J. Pediatr. 98:696-701.

Greer, F.R., Steichen, J.J. and Tsang, R.C. (1982). Calcium and phosphate supplements in breast milk-related rickets. Am. J. Dis. Child. 136:581-583.

Guggenheimer, J., Nowak, A.J. and Michaels, R.H. (1971). Dental manifestations of the rubella syndrome. Oral Surg. 32:30-37.

Gutbeilet, R.L. and Cornblath, M. (1976). Neonatal hypoglycaemia revisited. Pediatrics, 58:1-17.

Hall, R.K. (1959). Gross tooth hypocalcification in vitamin D resistant rickets. Aust. Dent. J. 4:329-330.

Hals, E. (1962). Dentine and enamel anomalies: histologic observations. In Witkop, C.H. (ed.) Genetics and dental health. New York: McGraw-Hill, pp 246-260.

Harris, R. and Sullivan, H.R. (1960). Dental sequelae in deciduous dentition in vitamin D resistant rickets. Case report. Aust. Dent. J. 5:200-203.

Hatch, D.J. (1968). Prolonged nasotracheal intubation in infants and children. Lancet 1:1272-1275.

Hathaway, W.E. (1970). Coagulation problems in the newborn infant. Pediatr. Clin. N. Amer. 17:929-942.

Henry, P.J. (1969). Mouth guards in general anaesthesia. Med. J. Aust. 1:911-912.

Herman, S.C. and McDonald, R.E. (1963). Enamel hypoplasia in cerebral palsied children. J. Dent. Child. 30:46-49.

Hillman, L.S. and Haddad, J.G. (1975). Perinatal vitamin D metabolism. J. Pediatr. 86:923-935.

Hinrichs, E.H. (1956). Dental changes in idiopathic juvenile hypoparathyroidism. Oral Surg. 9:1102-1114.

Hobel, D.H., Hyvariner, M., Okada, D. and Oh, W. (1973). Prenatal and intrapartum high risk screening: Prediction of the high risk neonate. Am. J. Obstet. Gynaecol. 117:1-9.

Ideberg, M. and Persson, B. (1971). Development of permanent tooth germs involved in mandibular fractures in children. J. Dent. Res. 50:721.

Infante, P.F. and Gillespie, G.M. (1977). Enamel hypoplasia in relation to caries in Guatemalan children. J. Dent. Res. 56:493-498.

James, L.S. (1964). Onset of breathing and resusitation. J. Pediatr. 65:807-815.

Jelliffe, D.B., Jelliffe, E.F.P., Garcia, I. and De Barrios, G. (1961). The children of the San Blas Indians of Panama. J. Pediatr. 59:271-276.

Jordan, W.S., Graves, C.L. and Elwyn, R.A. (1970). New therapy for postintubation laryngeal edema and tracheitis in children. J. A. M. A. 212:585-588.

Joshi, V.V., Mandaria, S.G. and Wiglesworth, F.W. (1972). Acute lesions induced by endotracheal intubation. Am. J. Dis. Child. 124:646-649.

Jung, A.L. and Thomas, G.K. (1974). Stricture of nasal vestibule: A complication of nasotracheal intubation in newborn infants. J. Pediatr. 85:412-414.

Karpartkin, M. (1971). Diagnosis and management of disseminated intravascular coagulation. Pediatr. Clin. N. Amer. 18:23-28.

Kitterman, J.A., Edmunds, L.H. and Gregory, G.A. (1972). Patent ductus arteriosus in premature infants: Incidence, relation to pulmonary disease and management. N. Engl. J. Med. 287:473-477.

Kodicek, E. (1974). The story of vitamin D: From vitamin to hormone. Lancet 1:326-330.

Korkhaus, G.A. (1930). A new orthodontic symmetrograph. Intern. J. Ortho. 16:665-679.

Kraus, B.S. and Jordan, R.E. (1965). The human dentition before birth. Philadelphia: Lea and Febiger.

Kreshover, S.J. and Clough, D.W. (1953). Prenatal influences on tooth development. II. Artificially induced fever in rats. J. Dent. Res. 32:565-577.

Kreshover, S.J., Clough, D.W. and Bear, D.M. (1958). A study of prenatal influences on tooth development in humans. J. Amer. Dent. Ass. 56:230-248.

Kreshover, S.J. (1960). Metabolic disturbances in tooth formation. Ann. N. Y. Acad. Sci. 85:161-167.

Kronfeld, R. and Schour, I. (1939). Neonatal dental hypoplasia. J. Amer. Dent. Ass. 26:18-32.

Krous, H. (1980). Defective dentition following mechanical ventilation. Letter to the Editor. J. Pediatr. 97:334.

Kubli, F.W. and Kaeser, O. (1969). Diagnostic management of chronic placental insufficiency. In Pecile, A. and Finzi, C. (eds). The feto-placental unit. Amsterdam: Exerpta Medica Foundation, pp 10-12.

Lakdawala, D.R. and Widdowson, E.M. (1977). Vitamin D in human milk. Lancet 1:167-168.

Lapatsanis, P. Deliyanni, V. and Doxiadis, S. (1968). Vitamin D deficiency rickets in Greece. J. Pediatr. 73:195-202.

Larsson, E. (1972). Dummy and finger-sucking habits with special attention to their significance for facial growth and occlusion. Swed. Dent. J. 65:605-634.

Lawson, B.F. and Stout, F.W. (1971). The incidence of enamel hypoplasia associated with chronic lead poisoning. S. C. Dent. J. 29:5-10.

Leatherwood, E.C., Burnett, G.W., Chandravyjsmarn, R. and Sirikaya, O. (1965). Dental caries and dental fluorosis in Thailand. Am. J. Pub. Health 55:1792-1799.

Lebret, L. (1962). Growth changes of the palate. J. Dent. Res. 41:1391-1404.

Lenstrup, K. (1955). On injury by factures of the jaws to teeth in course of formation. Acta odont. Scand. 13:181-202.

Levin, R.S. and Keen, J.H. (1974). Neonatal enamel hypoplasia in association with symptomatic neonatal hypocalcaemia. Brit. Dent. J. 137:429-432.

Lewin, P.K., Reid, M., Reilly, B.J., Swyer, P.R. and Fraser, D. (1971). Iatrogenic rickets in low birth weight infants. J. Pediatr. 78:207-210.

Logan, W.H.G. and Kronfeld, R. (1933). Development of the human jaws and surrounding structures from birth to age of fifteen years. J. Amer. Dent. Ass. 20:379-382.

Losch, P., Brown, J.C. and Boyle, P.E. (1940). Discolouration of teeth in haemolytic disease. J. Dent. Res. 19:293-297.

Lunt, R.C. and Law, D.B. (1974). A review of the chronology of eruption of deciduous teeth. J. Amer. Dent. Ass. 89:872-879.

Magnusson, B.O. (1981). Pedodontics: A systematic approach. Copenhagen: Munksgaard, pp 92-93.

Marks, S.C., Lindahl, R.Y. and Bowden, J.W. (1965). Dental and cephalometric findings in vitamin D resistant rickets. J. Dent. Child. 32:259-265.

Masel, J.P., Tudehope, D., Cartwright, D., Cleghorn, G. (1982). Osteopenia and rickets in the extremely low birth weight infant - A survey of the incidence and radiological classification. Aust. Radiol. 26:83-96.

McCormack, J. and Filostrat, D.J. (1967). Injury to the teeth of succession by abscess of the temporary teeth. J. Dent. Child. 34:501-504.

McDonald, R.E. and Avery, D.R. (1978). Dentistry for the child and adolescent. St Louis: C.V. Mosby, pp 45-69.

Mellanby, M. (1937). The structure of dental tissues with special reference to some stages in the development of normal and hypoplastic enamel. Brit. Dent. J. 63:557-563.

Mellanby, M. (1941). The effect of maternal dietary deficiency of vitamin A on dental tissues in rats. J. Dent. Res. 20:489-509.

Mellander, M., Noren, J.G., Freden, A. and Kjellmer, I. (1982). Mineralisation defects in deciduous teeth of low birth weight infants. Acta Paed. Scand. 71:727-733.

Milhorat, T.H. (1981). Disorders of neurological importance. In Avery, G.B. (ed.) Neonatalogy. Philadelphia: Lippincott, pp 964-986.

Miller, J. (1951). Pigmentation of teeth due to Rhesus factor. Brit. Dent. J. 91:121-123.

Miller, J. and Forrester, R.M. (1959). Neonatal enamel hypoplasia. Brit. Dent. J. 106:93-104.

Mink, J.R. (1959). Relationship of hypoplastic teeth and surgical trauma in cleft repair. J. Dent. Res. 38:652-653.

Minoguchi, G. (1970). Japanese studies on water and food fluoride and general health. In Fluorides and human health. Geneva: W. H. O. pp 294-304.

Minton, S.D. and Steichen, J.J. (1979). Bone mineral content in term and preterm appropriate for gestational age infants. J. Pediatr. 95:1037-1042.

Moller, I.J. and Poulsen, S. (1975). A study of dental mottling in children in Khouribga, Morocco. Arch. Oral Biol. 20:601-607.

Moylan, F.M.B., Selden, E.B., Shannon, D.C. and Todres, J.D. (1980). Defective primary dentition in survivors of neonatal mechanical ventilation. J. Pediatr. 96:106-108.

Musselman, R.J. (1968). Dental defects and rubella embryopathy: A clinical study of fifty children. J. Amer. Dent. Ass. 50:536-538.

Naiman, J.L. (1972). Current management of haemolytic disease of the newborn infant. J. Pediatr. 80:1049-1059.

Nanda, R.S., Zipkin, I., Doyle, J. and Horowitz, H.S. (1974). Factors affecting the prevalence of dental fluorosis in Lucknow, India. Arch. Oral Biol. 19:781-792.

Noren, J.G., Odelius, B., Rosander, B. and Linde, A. (1984). SIMS Analysis of deciduous enamel from normal full-term infants, low birth weight infants and from infants with congenital hypothyroidism. Caries Res. 18:242-249.

Nowak, A.J. and Erenberg, A. (1982). Palatal and alveolar ridge grooves in orotracheal intubated neonates. Personal Communication.

Nylen, M.U., Omnell, K. and Lofgren, C. (1972). An election microscopic study of tetracycline-induced enamel defects in rat incisor enamel. Scand. J. Dent. Res. 80:384-409.

Oski, F.A. (1981). Haemolytic problems. In Avery, G.B. (ed.) Neonatalogy. Philadelphia: Lippincott, pp 545-582.

Owen, L.N. (1963). The effects of administering tetracyclines to young dogs with particular reference to localisation of the drugs in the teeth. Arch. Oral Biol. 8:715-717.

Perlstein, M.A. and Massler, M. (1956). Prenatal dental enamel dysplasia with special reference to its occurrence in kernicterus. Amer. J. Phys. Med. 35:324-330.

Pindborg, J.J. (1970). Pathology of hard tissues. Philadelphia: W.B. Saunders, pp 88-89.

Pisanty, S. and Garfunkel, A. (1977). Familial hypoparathyroidism with candidiasis and mental retardation. Oral Surg. 44:374-383.

Pliskin, M.E., Brown, A.M., Baden, E.E. and Kimball, H.G. (1975). Vitamin D resistant rickets of a young adult patient. J. Oral Med. 30:77-80.

Powell, J.B. and Keown, K.K. (1965). Endotracheal aspiration of a tooth. Anaesth. Analg. Curr. Res. 44:355-357.

Poznanski, A.K., Kuhns, L.R. and Guire, K.E. (1980). New standards of cortical mass in the humerus of neonates: A means of evaluating bone loss in the premature infant. Radiology 134:639-644.

Pu, M.Y. and Lilienthal, B. (1961). Dental caries and mottled enamel among Formosan children. Arch. Oral Biol. 5:125-136.

Purvis, R.J., Mackay, G.S., Cockburn, F., Barrie, W.J., Williamson, E.M., Belton, N.R. and Forfar, J.O. (1973). Enamel hypoplasia of the teeth associated with neonatal tetany: A manifestation of maternal vitamin D deficiency. Lancet 2:811-814.

Puschett, J.B., Morantz, J. and Kurnick, W.S. (1972). Evidence for a direct action of cholecalciferol and 25-hydroxycholecalciferol on the renal transport of phosphate, sodium and calcium. J. Clin. Invest. 51:373-385.

Queenan, J.T. (1977). Modern management of the Rh problem. Hagerstown: Harper and Row.

Rao, S. and Witkop, C.J. (1971). Inherited defects in tooth structure. In Bergsma, D. (ed.) XI. Orofacial structures. Birth Defects. 7:153-160.

Ravn, J.J. (1975). Developmental disturbances in permanent teeth after exarticulation of their primary predecessor. Scand. J. Dent. Res. 83:131-134.

Ravn, J.J. (1976). Developmental disturbances in permanent teeth after intrusion of their primary predecessors. Scand. J. Dent. Res. 84:137-141.

Rasmussen, J. (1974). Parathyroid hormone, calcitonin and the calciferols. In Williams, R.H. (ed.). Textbook of endocrinology. Philadelphia: W.B. Saunders, pp 663-773.

Redman, R.S., Shapiro, B.L. and Gorlin, R.J. (1966). Measurement of normal and reportedly malformed palatal vaults. II Normal juvenile measurements. J. Dent. Res. 45:266-269.

Ridell, A. and Astrand, P. (1971). Conservation treatment of teeth involved by mandibular fractures. Swed. dent. J. 64:623-632.

Ritchie, G. (1965). Dental manifestations of pseudohypoparathyroidism. Arch. Dis. Child. 40:565-572.

Roholm, K. (1937). Fluorine intoxication. A clinical-hygienic study. Copenhagen: Nyt Nordisk Forlag, pp 1-15.

Root, A.W. and Harrison, H.E. (1976). Recent advances in calcium metabolism. J. Pediatr. 88:1-18.

Rosenberg, M. and Bolgla, J. (1968) Protection of teeth and gums during endotracheal intubation. Anaesth. Analg. Curr. Res. 47:34-36.

Rosenthal, I.M. (1983). Metabolic bone diseas. In Behrman, R.E. and Vaughan, J.C. (eds). Nelson textbook of pediatrics. Philadelphia: W.B. Saunders, p. 1653.

Rosenzweig, K.A. and Sahar, M. (1962). Enamel hypoplasia and dental caries in the primary dentition of prematuri. Brit. Dent. J. 113:279-280.

Rule, J.T. (1972). The relationship between ankylosed primary molars and multiple enamel defects. J. Dent. Child. 39:29-35.

Rushton, M.A. (1933). Fine contour lines of enamel of milk teeth. Dent. Rec. 53:170-171.

Sarnat, B.G. and Schour, I. (1942). Enamel hypoplasia (chronologic enamel aplasia) in relation to systemic disease: A chronologic, morphologic and etiologic classification. J. Amer. Dent. Assoc. 29:67-75.

Sauk, J.J. and Witkop, C.J. (1973). Election optic analysis of human dentine in hypophosphataemic vitamin D resistant rickets (Report of a kindred with consanguinity). J. Oral Path. 2:203-214.

Schour, I. and Kronfeld, R. (1938). Neonatal dental hypoplasia. J. Amer. Dent. Assoc. 26:18-32.

Schwachman, H. and Schuster, A. (1956). The tetracyclines; applied pharmacology. Pediatr. Clin. N. Amer. 3:295-303.

Scrimshaw, N.S., Taylor, C.E. and Gordon, J.E. (1968). Interactions of nutrition and infection. W.H.O. Monograph No. 57. Geneva: W.H.O.

Seino, Y., Ishii, T., Shimotsuji, T., Ishida, M. and Yabuuchi, J. (1981). Plasma active vitamin D concentration in low birth weight infants with rickets and its response to vitamin D treatment. Arch. Dis. Child. 56:628-632.

Senior, B. (1973). Current concepts: Neonatal hypoglycaemia. N. Engl. J. Med. 289:790-793.

Shapiro, B.L., Redman, R.S. and Gorlin, R.J. (1962). Measurement of normal and reportedly malformed palatal vaults. J. Dent. Res. 41:1039.

Shelling, D.H. and Anderson, G.M. (1936). Relation of rickets and vitamin D to the incidence of dental caries, enamel hypoplasia and malocclusion in children. J. Amer. Dent. Assoc. 23:840-846.

Shusterman, S. and Fellers, F.X. (1969). The prevalence of enamel defects in childhood nephrotic syndrome. J. Dent. Child. 36:435-440.

Slavkin, H.C. (1979). Developmental craniofacial biology. Philadelphia: Lea & Febiger.

Smith, D.M.H. and Miller, J. (1979). Gastroenteritis, coeliac disease and enamel hypoplasia. Brit. Dent. J. 147:91-95.

Smith, M.C. and Smith, H.V. (1935). The occurrence of mottled enamel on the temporary teeth. J. Amer. Dent. Assoc. 22:814-817.

Soni, N.N. and Marks, S.C. (1967). Microradiographic and polarised-light study of dental tissues in vitamin D resistant rickets. Oral Surg. 23:755-762.

Sperber, G.H. (1967). Enamel hypoplasia. Oral Surg. 24:50-51.

Steichen, J.J., Tsang, R.C., Gratton, T.L., Hamstra, A. and De Luca, H.F. (1980). Vitamin D homeostasis in the perinatal period. N. Engl. J. Med. 302:315-319.

Steichen, J.J., Gratton, T.L. and Tsang, R.C. (1980). Osteopenia of prematurity: the cause and possible treatment. J. Pediatr. 96:528-534.

Steichen, J.J., Tsang, R.C., Greer, F.R., Ho, M. and Hug, G. (1981). Elevated serum 1,25 dihydioxyvitamin D concentration in rickets of very-low-birth-weight infants. J. Pediatr. 99:293-298.

Stein, G. (1936). Enamel defects in deciduous dentition and their clinical significance. J. Amer. Dent. Ass. 26:18-22.

Stein, G. (1947). Enamel damage of systemic origin in premature birth and diseases of early infancy. Amer. J. Ortho. 33:831-841.

Stern, L. and Denton, R.L. (1965). Kernicterus in small premature infants. Pediatrics, 35:483-485.

Stewart, R.E., Barber, T.K., Troutman, K.C. and Wei, S.H.Y. (1982). Pediatric Dentistry. Scientific foundations and clinical practice. St Louis: C.V. Mosby, pp 87-134.

Stimmler, L. Snodgrass, G.J.A.I. and Jaffe, E. (1973). Dental defects associated with neonatal symptomatic hypocalcaemia. Arch. Dis. Child. 48:217-220.

Sweeney, E.A., Cabbrera, J., Urrutia, J. and Mata, L. (1969). Factors associated with linear hypoplasia of human deciduous incisors. J. Dent. Res. 48:1275-1279.

Sweeney, E.A., Saffir, A.J. and de Leon, R. (1971). Linear Hypoplasia of deciduous incisor teeth in malnourished children. Amer. J. Clin. Nutr. 24:29-31.

Swyer, P. (1981). The organisation of perinatal care with particular reference to the newborn. In Avery, G.B. (ed.) Neonatalogy. Philadelphia: J.B. Lippincott, pp 17-47.

Tank, G. (1951). Two cases of green pigmentation of the deciduous teeth associated with hemolytic disease of the newborn. J. Amer. Dent. Ass. 42:302-306.

Thursfield, J. (1912). Pigmentation of teeth from haemolytic disease. Proc. Roy. Soc. Med. (Disease Child.) 5:147-152.

Towbin, A. (1968). Cerebral intravenricular haemorrhage and subependymal matrix infarction in the fetus and premature newborn. Amer. J. Pathol. 52:121-140.

Tracey, W.E. and Campbell, R.A. (1968). Dentofacial development in children with vitamin D resistant rickets. J. Amer. Dent. Ass. 76:1026-1031.

Tsang, R.C., Light, I.J., Sutherland, J.M. and Kleiman, L.I. (1973). Possible pathogenetic factors in neonatal hypocalcaemia of prematurity: The role of gestation, hyperphosphataemia, hypomagnesaemia, urinary calcium loss and parathormone responsiveness. J. Pediatr. 82:423-429.

Tsang, R.C., Chen, I.W. and Friedman, W.A.(1974). Functional hypoparathyroidism in neonatal hypocalcaemia of infant of diabetic mother. Pediatr. Res. 8:377A.

Tsang, R.C., Chen, I.W., Hayes, W., Atkinson, W., Atherton, H. and Edwards, N. (1974). Neonatal hypocalcaemia in infants with birth asphyxia. J. Pediatr. 84:428.

Tsang, R.C., Chen, I.W., Friedman, M.A., Gigger, M. and Steichen, J.J. (1975). Parathyroid function in infants of diabetic mothers. J. Pediatr. 86:399-404.

Tsang, R.C., Donovan, E.F. and Steichen, J.J. (1976). Calcium physiology and pathology in the neonate. Pediatr. Clin. N. Am. 23:611-626.

Tsang, R.C. and Steichen, J.J. (1977). Perinatal calcium homeostasis. Neonatal hypocalcaemia and bone demineralisation. Clin. Perinatol. 43:385-409.

Tsang, R.C. (1983). The quandary of vitamin D in the newborn infant. Lancet 1:1370-1372.

Tudehope, D.I., Burns, Y., O'Callaghan, M. and Mohay, H. (1981). Minor neurological abnormalities during the first year of life of infants of birth weight <1500g. Aust. Paediatr. J. 17:265-268.

Tudehope, D.I., Burns, Y., O'Callaghan, M., Mohay, H. and Silcock, A. (1983). The relationship between intrauterine and postnatal growth on the subsequent psychomotor development of very-low-birth-weight infants. Aust. Paediatr. J. 13:3-10.

Turner, J.G. (1912). Two cases of hypoplasia of enamel. Br. J. Dent. Sci. 55:227-228.

Usher, R.H., Allen, A.C. and McLean, F.H. (1971). Risk of respiratory distress syndrome related to gestational age, route of delivery and maternal diabetes. Am. J. Obstet. Gynaecol. 111:826-832.

Usher, R.H. (1981). The special problems of the premature infant. In Avery, C.B. (ed.). Neonatology. Philadelphia: Lippincott, pp 230-259.

Van der Linden, F.P.G.M. (1978). Changes in the position of posterior teeth in relation to ruga points. Am. J. Ortho. 74:142-161.

Via, W.F. and Churchill, J.A. (1959). Relationship of enamel hypoplasia to abnormal events of gestation and birth. J. Amer. Dent. Ass. 59:702-707.

Via, W.F. (1967). Spontaneous degeneration of the dental pulp associated with phsophate diabetes. Oral Surg. 24:623-627.

Wasmuth, C.E. (1960). Legal pitfalls in the practice of anaesthesiology. Part 2. Complications of endotracheal anaesthesia. Anaesth. Analg. Curr. Res. 39:138-140.

Watson, A.O. (1955). Infantile cerebral palsy. Dent. J. Aust. 27:6-14.

Weinmann, J.P., Svoboda, J.F. and Woods, R.W. (1945). Hereditary disturbances of enamel formation and calcification. J. Amer. Dent. Ass. 32:397-418.

Weinstock, A. (1972). Matrix development in mineralising tissues as shown by radioautography: formation of enamel and dentine. In Slavkin, H.C. (ed.). Developmental aspects of oral biology. New York: Academic Press. pp 30-46.

Weisman, Y. (1976). Perinatal metabolism of vitamin D in the rat. Pediatr. Res. 10:693-706.

Weiss, M.B. (1963). The cause of white opaque areas in permanent teeth. J. Dent. Child. 30:154-160.

Wetzel, R.C. (1980). Defective dentition following mechanical ventilation. Letter to the Editor. J. Pediatr. 97:334.

Weyman, J. (1968). The effect of irradiation on developing teeth. Oral Surg. 25:623-629.

Wihr, N.L. (1970). Abnormal dentition in vitamin D resistant rickets: a case report. J. Dent. Child. 37:333-334.

Williamson, J.J. (1966). Trauma during exodontia: An aetiologic factor in hypoplastic premolars. Brit. Dent. J. 121:284-289.

Wilson, M.G. and Mikity, V.G. (1960). A new form of respiratory disease in premature infants. Am. J. Dis. Child. 99:489-499.

Winter, G.B. and Brook, A.H. (1975). Enamel hypoplasia and anomalies of enamel. In Poole, A.E. (ed.). Symposium on genetics. Dent. Clin. N. Am. 19:3-24.

Witkop, C.J. (1975). Hereditary defects of dentine. Dent. Clin. N. Am. 19:25-45.

Woodhead, J.C., Nowak, A.J., Crall, J.J. and Robillard, J.E. (1982). Dental abnormalities in children with chronic renal failure. Pediatr. Dent. 4:281-285.

Woodward, W.E., Hirschhorn, H., Sack, R.B., Cash, R.A., Brownlee, I., Chickadonz, G.H., Evans, L.K., Shepard, R.H. and Woodward, R.C. (1974). Acute diarrhoea on an Apache Indian reservation. Amer. J. Epidemiol. 99:281-290.

Appendix 1

Mater Misericordiae Childrens Hospital

South Brisbane, Queensland 4101 Phone 240 8111

Dear

We invite you to participate in a dental examination, now being offered to children of the Growth and Development Clinic at the Mater Hospital. The examination is part of a research study conducted by the division of children's dentistry, Dental School, University of Queensland. The aim of the study is to detect abnormalities of the teeth associated with low birth weights in children. Early diagnosis of these abnormalities may lead to the prevention of further problems.

The examination will be carried out by John P. Brown and Kim Seow, University staff dentists specialising in dentistry for children, who will be happy to discuss your child's dental condition with you then. X-rays will not be taken unless a particular need is evident.

Details of an appointment made for you and your child are shown below.

I would appreciate your attendance for this dental examination.

Yours sincerely,

Dr. D. Tudehope,
Director of Neonatology,
Mater Hospital.

Dr. John P. Brown,
Senior Lecturer in
Dentistry for Children,
University of Queensland.

An appointment has been made for _____ at the University of Queensland Dental School, Turbot Street, Brisbane*.

_____ a.m./p.m. _____ _____ 19____.

Would you phone to confirm this time or if this time does not suit or if you have any questions, please call Kim Seow on 221 8044 Ext: 59.

* Please use the entrance opposite the SGIO Theatre and proceed to Clinic 6, on the 2nd Floor.

APPENDIX 2

NAME: ..... SEX .....

ADDRESS: ..... PHOTOGRAPHS .....

..... X-RAYS .....

D.O.B.: .....

DATE OF EXAM: .....AGE AT EXAM: .....

MATERNAL HISTORY

Maternal Age at Birth .....

F in pregnancy : F water: .....
Supplement: ..... Dosage ..... Regular/Irregular ....

Maternal Bleeding ..... Infection .....

Toxaemia ..... Severe trauma .....

Diabetes .....Medications .....

1st trimester X-ray .....Rh incompatibility .....

Other .....

NEONATAL HISTORY

Gestational Age: .... Wt. at birth .....

Intubation: ..... Oral ..... Nasal ..... How long .....

.....

Difficult Birth .....

Rickets .....

Respiratory difficulties .....

Severe jaundice ..... Hypoglycaemia .....

Tetany ..... Seizures .....

Infections ..... Other .....

POST NATAL HISTORY

Family dentist: .....

Dental History: .....

.....

F intake: ..... Started ..... Forms ..... Dosage .....
Stopped .....

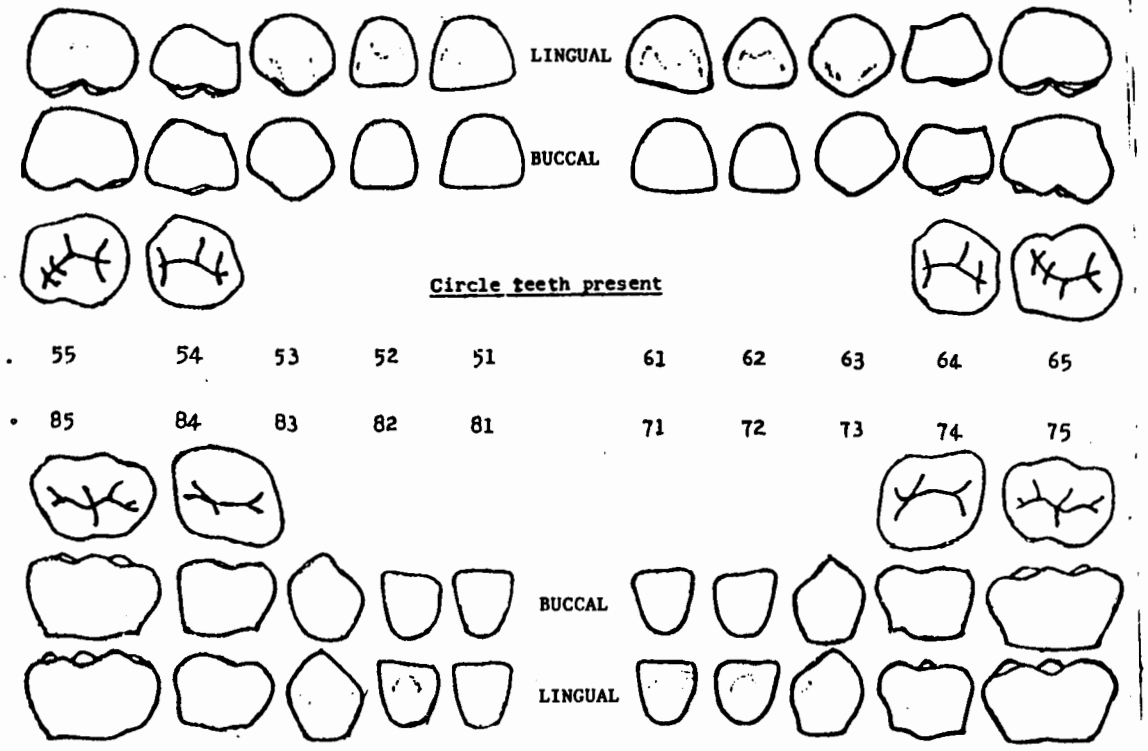
Oral trauma:.....

Severe infections ..... Mumps .....

Measles ..... Chicken pox .....

Other .....

Appendix 3



Name:

D.o.b.:

Occlusion

Distal step:

Straight:

Mesial step:

Spaced:

Unspaced:

Palate

Groove:

Side:

Nasal Deformity

Present:

Side:

C=Caries (blue)
1. White Spot
2. Cavitation
3. Severe Destruction

O=Opacities White/brown Intact
1. Mild
2. Mod
3. Severe

H = Hypoplasia Ridging, Pitting or Surface Irregularity
1. Mild
2. Mod
3. Severe

F=Fluorosis
Q. Questionable
1. Very Mild
2. Mild
3. Mod (stain/hypo)